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(71) Applicant: AORTECH EUROPE LIMITED [GB/GB];
Phoenix Crescent, Strathclyde Business Park, Bellshill
ML4 3NJ (GB).

(72) Inventors: O'CONNOR, Bernard; 56 Braidwood Road,
Braidwood, South Lanarkshire ML8 5NY (GB). HA-
WORTH, William, Stafford; Broomlands House, 31
Main Street, Symington, Biggar ML12 6LL (GB).

(74) Agent: MURGITROYD & COMPANY; Scotland
House, 165-169 Scotland Street, Glasgow G5 8PL (GB).

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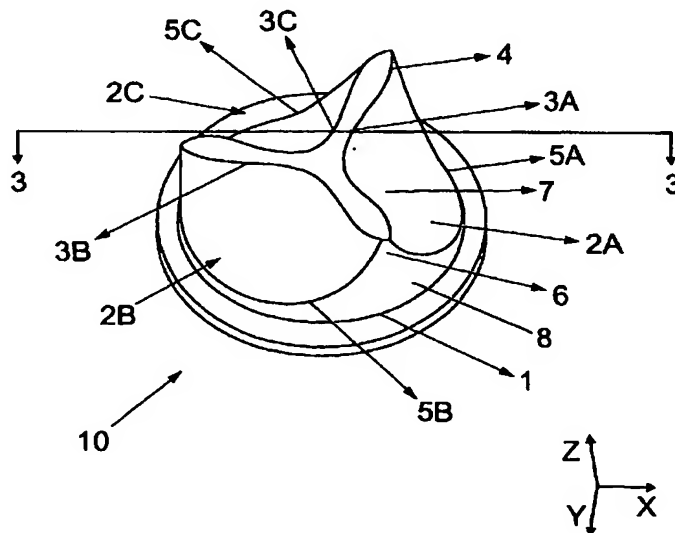
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(54) Title: HEAT VALVE PROSTHESIS AND METHOD OF MANUFACTURE



(57) Abstract: The present invention provides a cardiac valve prosthesis comprising a frame (1) and two or more leaflets (2a, 2b) (preferably three) attached to the frame. The leaflets are attached to the frame between posts (8), with a free edge (3a, 3b) which can seal the leaflets together when the valve is closed under back pressure. The leaflets are created in a mathematically defined shape allowing good wash-out of the whole leaflet orifice, including the area close to the frame posts, thereby relieving the problem of thrombus deposition under clinical implant conditions.



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11 **HEART VALVE PROSTHESIS AND METHOD OF MANUFACTURE**

12

13 **FIELD OF THE INVENTION**

14

15 The present invention relates to medical
16 implants, particularly cardiac and vascular implants
17 and prostheses. More specifically, the invention
18 relates to a cardiac valve prosthesis comprising a
19 frame and leaflets. Such valves may also be made
20 without rigid frames and may also be used as valves
21 in artificial hearts, whether the latter are intended
22 for permanent implantation or for temporary support
23 of a patient.

24

25 **BACKGROUND OF THE INVENTION**

26 In mammals the heart is the organ responsible
27 for maintaining an adequate supply of blood, and
28 hence of oxygen and nutrients, to all parts of the
29 body. Reverse flow of blood through the heart is
30 prevented by four valves which serve as the inlet and

1 outlet of each of the two ventricles, the pumping
2 chambers of the heart.

3 Dysfunction of one or more of these valves can
4 have serious medical consequences. Such dysfunction
5 may result from congenital defects, or from disease
6 induced damage. Forms of dysfunction include stenosis
7 (reduction in the orifice of the open valve) and
8 regurgitation (reverse flow through the closing or
9 closed valve), either of which increases the work
10 required by the heart to maintain the appropriate
11 blood flows to the body.

12 In many cases the only effective solution is to
13 replace the malfunctioning valve. A valve replacement
14 operation is expensive and requires specialised
15 facilities for open heart surgery. Replacement of
16 failed artificial heart valves carries increased risk
17 over the initial replacement, so there are practical
18 limits on the number of times reoperation can be
19 undertaken. Consequently, the design and materials of
20 an artificial valve must provide for durability of
21 the valve in the patient. The artificial valve must
22 also operate without high pressure gradients or undue
23 reverse flow during closing or when closed, because
24 these are the very reasons for which a replacement of
25 the natural valve is undertaken.

26 Mechanical valves, which use a ball or a disc or
27 a pair of pivoting rigid leaflets as the opening
28 member(s) can meet these combined requirements of
29 haemodynamic performance and durability.
30 Unfortunately, a patient who has had a mechanical
31 valve implanted must be treated with anticoagulants,

1 otherwise blood will clot on the valve. Clotting on
2 the valve can either restrict the movement of the
3 valve opening member(s), impairing valve function, or
4 can break free from the valve and obstruct blood
5 vessels downstream from the valve, or both. A patient
6 receiving a mechanical valve will be treated with
7 anticoagulants for life.

8 Valves excised from pigs and treated with
9 glutaraldehyde to crosslink and stabilise the tissue
10 are also used for replacement of defective valves.
11 These may be mounted on a more or less rigid frame,
12 to facilitate implantation, or they may be unmounted
13 and sewn by the surgeon directly to the vessel walls
14 at operation. A further type of valve replacement is
15 constructed from natural tissue, such as pericardium,
16 treated with glutaraldehyde and mounted on a frame.
17 Valves from pigs or made from other animal or human
18 tissue are collectively known as tissue valves. A
19 major advantage of tissue valves over mechanical
20 valves is that they are much less likely to provoke
21 the blood to clot, and so patients receiving tissue
22 valves are not normally given anticoagulants other
23 than during the immediate post operative period.
24 Unfortunately, tissue valves deteriorate over time,
25 often as a result of calcification of the crosslinked
26 natural tissue. This deterioration presents a
27 problem, particularly in young patients. Thus,
28 although the recipient of a tissue valve is not
29 required to take anticoagulants, the durability of
30 tissue valves is less than that of mechanical valves.

1 In third world countries, where rheumatic fever
2 is still common, the problems of valve replacement in
3 young patients are considerable. Anticoagulants,
4 required for mechanical valves, are impractical and
5 accelerated calcification of tissue valves precludes
6 their use.

7 In the Western world, life expectancy continues
8 to increase, and this results in a corresponding rise
9 both in patients requiring cardiac valve replacement,
10 and in those patients needing replacement of
11 deteriorating artificial valves implanted in the
12 past. There is, therefore, a need for a replacement
13 heart valve with good haemodynamics, extended
14 durability and having sufficiently low risk of
15 inducing clotting so that anticoagulants are not
16 necessary.

17 The natural heart valves use thin flexible
18 tissue leaflets as the closing members. The leaflets
19 move readily out of the orifice as blood begins to
20 flow through the valve so that flow through the open
21 valve is unrestricted by the leaflets. Tissue valves
22 function similarly, providing a relatively
23 unrestricted orifice when the valve is open. For
24 mechanical valves, on the other hand, the closing
25 member rotates in the orifice, but is not removed
26 from the orifice when the valve opens. This provides
27 some restriction to flow, but, more importantly,
28 disturbs the blood flow patterns. This disturbance to
29 the flow is widely held to initiate, or at least to
30 contribute significantly to, the observed tendency of
31 mechanical valves to produce clotting.

1 A number of trileaflet polyurethane valve
2 designs have been described.

3 A valve design, comprising a leaflet geometry
4 which was elliptical in the radial direction and
5 hyperbolic in the circumferential direction in the
6 closed valve position, with leaflets dip-coated from
7 non-biostable polyurethane solutions onto injection-
8 moulded polyurethane frames has attained durabilities
9 in excess of 800 million cycles during *in vitro*
10 fatigue testing (Mackay TG, Wheatley DJ, Bernacca GM,
11 Hindle CS, Fisher AC. New polyurethane heart valve
12 prosthesis: design, manufacture and evaluation.
13 *Biomaterials* 1996; 17:1857-1863; Mackay TG, Bernacca
14 GM, Wheatley DJ, Fisher AC, Hindle CS. *In vitro*
15 function and durability assessment of a polyurethane
16 heart valve prosthesis. *Artificial Organs* 1996;
17 20:1017-1025; Bernacca GM, Mackay TG, Wheatley DJ. *In*
18 *vitro* function and durability of a polyurethane heart
19 valve: material considerations. *J Heart Valve Dis*
20 1996; 5:538-542; Bernacca GM, Mackay TG, Wilkinson R,
21 Wheatley DJ. Polyurethane heart valves: fatigue
22 failure, calcification and polyurethane structure. *J*
23 *Biomed Mater Res* 1997; 34:371-379; Bernacca GM,
24 Mackay TG, Gulbransen MJ, Donn AW, Wheatley DJ.
25 Polyurethane heart valve durability: effects of
26 leaflet thickness. *Int J Artif Organs* 1997; 20:327-
27 331.). However, this valve design became
28 unacceptably stenotic in small sizes. Thus, a
29 redesign was effected, changing the hyperbolic angle
30 from the free edge to the leaflet base, and replacing
31 the injection-moulded frame with a rigid, high

1 modulus polymer frame. This redesign permitted the
2 use of a thinner frame, thus increasing valve orifice
3 area. This valve design, with a non-biostable
4 polyurethane leaflet material, was implanted in a
5 growing sheep model. Valve performance was good over
6 the six month implant period, but the region close to
7 the frame posts on the inflow side of the valve, at
8 which full leaflet opening was not achieved, suffered
9 a local accumulation of thrombus (Bernacca GM, Raco
10 L, Mackay TG, Wheatley DJ. Durability and function of
11 a polyurethane heart valve after six months *in vivo*.
12 Presented at the XII World Congress of International
13 Society for Artificial Organs and XXVI Congress of
14 the European Society for Artificial Organs,
15 Edinburgh, August 1999. Wheatley DJ, Raco L,
16 Bernacca GM, Sim I, Belcher PR, Boyd JS.
17 Polyurethane: material for the next generation of
18 heart valve prostheses? *Eur. J. Cardio-Thorac. Surg.*
19 2000; 17; 440-448). This valve design used non-
20 biostable polyurethane, which had tolerable
21 mechanical durability, but which showed signs of
22 polymer degradation after six months *in vivo*.
23 International Patent Application WO 98/32400
24 entitled "Heart Valve Prosthesis" discloses a similar
25 design, i.e. closed leaflet geometry, comprising
26 essentially a trileaflet valve with leaflets moulded
27 in a geometry derived from a sphere towards the free
28 edge and a cone towards the base of the leaflets. The
29 spherical surface, defined by its radius, is intended
30 to provide a tight seal when the leaflets are under
31 back pressure, with ready opening provided by the

1 conical segment, defined by its half-angle, at the
2 base of the leaflets. Were the spherical portion
3 located at the leaflet base it is stated that this
4 would provide an advantage in terms of the stress
5 distribution when the valve is closed and under back
6 pressure.

7 U.S. Patent No. 5,376,113 entitled "Closing
8 Member Having Flexible Closing Elements, Especially a
9 Heart Valve" issued December 27, 1994 to Jansen et
10 al. discloses a method of producing flexible heart
11 valve leaflets using leaflets attached to a base ring
12 with posts extending from this upon which the
13 leaflets are mounted. The leaflets are formed with
14 the base ring in an expanded position, being
15 effectively of planar sheets of polymer, which become
16 flaccid on contraction of the ring. The resulting
17 valve is able to maintain both a stable open and a
18 stable closed position in the absence of any
19 pulsatile pressure, though in the neutral unloaded
20 position the valve leaflets contain bending stresses.
21 As a consequence of manufacturing the valve from
22 substantially planar sheets, the included angle
23 between the leaflets at the free edge where they
24 attach to the frame is 60° for a three leaflet valve.

25 U.S. Patent No. 5,500,016 entitled "Artificial
26 Heart Valve" discloses a valve having a leaflet shape
27 defined by the mathematical equation $z^2 + y^2 = 2RL$
28 $(x-g) - \alpha(x-g)^2$, where g is the offset of the leaflet
29 from the frame, RL is the radius of curvature of the
30 leaflet at $(g,0,0)$ and α is the shape parameter and
31 is >0 and <1 .

1 A valve design having a partially open
2 configuration when the valve is not subject to a
3 pressure gradient, but assuming a fully-open position
4 during forward flow is disclosed in International
5 Patent Application WO 97/41808 entitled "Method for
6 Producing Heart Valves". The valve may be a
7 polyurethane trileaflet valve and is contained within
8 a cylindrical outer sleeve.

9 U.S. Patent Nos. 4,222,126 and 4,265,694
10 disclose a trileaflet polyurethane valve with
11 integral polyurethane elastomeric leaflets having
12 their leading edges reinforced with an integral band
13 of polymer and the leaflets reinforced radially with
14 thicker lines of polyurethane.

15 The problem of chronic thrombus formation and
16 tissue overgrowth arising from the suture ring of
17 valves has been addressed by extension of the valve
18 body on either side of the suture ring as disclosed
19 in U.S. Patent No. 4,888,009 entitled "Prosthetic
20 Heart Valve".

21 Current polyurethane valve designs have a number
22 of potential drawbacks. Close coaptation of leaflets,
23 while ensuring good valve closure, limits the wash-
24 out of blood during haemodynamic function,
25 particularly in the regions close to the stent posts
26 at the commissures. This region of stagnation is
27 likely to encourage local thrombogenesis, with
28 further restriction of the valve orifice in the
29 longer term as well as increasing the risk of
30 material embolising into the circulation. Associated
31 with the thrombosis may be material degradation (in

1 non-biostable polyurethanes) and calcification
2 resulting in localised stiffening the leaflets,
3 stress concentrations and leaflet failure. As
4 previously discussed, animal implants of a trileaflet
5 polyurethane valve design have indicated that
6 thrombus does tend to collect in this region,
7 restricting the valve orifice and damaging the
8 structure of the valve.

9 Present valve designs are limited by the
10 availability of suitable polyurethanes which possess
11 good mechanical properties as well as sufficient
12 durability to anticipate clinical functionality of up
13 to twenty years or more. Many low modulus materials,
14 which provide good hydrodynamic function, fail during
15 fatigue testing at unacceptably low durations, due to
16 their greater susceptibility to the effects of
17 accumulated strain. Higher modulus polyurethanes may
18 be better able to withstand repeated stress without
19 accumulating significant damage, but are too stiff to
20 provide good hydrodynamic function in conventional
21 almost-closed geometry valve designs. Current design
22 strategies have not been directed towards enabling
23 the incorporation of potentially more durable, higher
24 modulus leaflet materials, nor the creation of a
25 valve design that is able to maintain good
26 hydrodynamic function with low modulus polyurethanes
27 manufactured as thick leaflets.

28 The nature of the valve leaflet attachment to
29 the frame is such that, in many valve designs, there
30 is a region of leaflet close to the frame, which is
31 restrained by the frame. This region may extend some

1 distance into the leaflet before it interfaces with
2 the free-moving part of the leaflet, or may be
3 directly at the interface between frame and leaflet.
4 There thus exists a stress concentration between the
5 area of leaflet that is relatively mobile, undergoing
6 transition between fully open and fully closed, and
7 the relatively stationary commissural region. The
8 magnitude of this flexural stress concentration is
9 maximised when the design parameters predicate high
10 bending strains in order for the leaflet to achieve
11 its fully open position.

12 U.S. Patent Nos. 4,222,126 and 4,265,694
13 disclose a valve which uses thickened leaflet areas
14 to strengthen vulnerable area of the leaflets.
15 However this approach is likely to increase the
16 flexure stress and be disadvantageous in terms of
17 leaflet hydrodynamic function.

18 The major difficulties which arise in designing
19 synthetic leaflet heart valves can be explained as
20 follows. The materials from which the natural
21 trileaflet heart valves (aortic and pulmonary) are
22 formed have deformation characteristics particularly
23 suited to the function of such a valve. Specifically,
24 they have a very low initial modulus, and so they are
25 very flexible in bending, which occurs at low strain.
26 This low modulus also allows the leaflet to deform
27 when the valve is closed and loaded in such a way
28 that the stresses generated at the attachment of the
29 leaflets, the commissures, are reduced. The leaflet
30 material then stiffens substantially, and this allows
31 the valve to sustain the closed loads without

1 prolapse. Synthetic materials with these mechanical
2 properties are not available.

3 Polyurethanes can be synthesised with good blood
4 handling and good durability. They are available with
5 a wide range of mechanical properties, although none
6 has as low a modulus as the natural heart valve
7 material. Although they show an increase in modulus
8 at higher strains, this does not occur until strains
9 much higher than those encountered in leaflet heart
10 valves.

11 Polyurethanes have been the materials of choice
12 for synthetic leaflet heart valves in the last decade
13 or more. More recently, polyurethanes have become
14 available which are resistant to degradation when
15 implanted. They are clearly more suitable for making
16 synthetic leaflet heart valves than non-stable
17 polyurethanes, but their use suffers from the same
18 limitations resulting from their mechanical
19 properties. Therefore, design changes must be sought
20 which enable synthetic trileaflet heart valves to
21 function with the best available materials.

22 Key performance parameters which must be
23 considered when designing a synthetic leaflet heart
24 valve include pressure gradient, regurgitation, blood
25 handling, and durability.

26 To minimise the gradient across the open valve,
27 the leaflets must open wide to the maximum orifice
28 possible, which is defined by the inside diameter of
29 the stent. This means that there must be adequate
30 material in the leaflets so they can be flexed into a
31 tube of diameter equal to the stent internal

1 diameter. In addition, there has to be a low energy
2 path for this bending because the pressure forces
3 available to open the valve are small, and the lower
4 the gradient, the smaller the pressure becomes. All
5 the leaflets must open for the lowest cardiac output
6 likely to be encountered by that valve in clinical
7 service.

8 To minimise closing regurgitation (reverse flow
9 lost through the closing valve) the valve leaflets
10 must be produced at or close to the closed position
11 of the valve. To minimise closed valve regurgitation
12 (reverse flow through the valve once it has closed),
13 the apposition of the leaflets in the commissural
14 region is found to be key, and from this perspective
15 the commissures should be formed in the closed
16 position.

17 Proper blood handling means minimising the
18 activation both of the coagulation system and of
19 platelets. The material of construction of the valve
20 is clearly a very important factor, but flow through
21 the valve must also avoid exposing blood either to
22 regions of high shear (velocity gradient) or to
23 regions of relative stasis. Avoiding regions of high
24 shear is achieved if the valve opens fully, and
25 relative stasis is avoided if the leaflet/frame
26 attachment and the commissural region in particular
27 opens wide. This is not achieved with typical
28 synthetic materials when the commissures are molded
29 almost closed, because the stiffness of synthetics is
30 too high.

1 Durability depends to a large extent on the
2 material of construction of the valve leaflets, but
3 for any given material, lifetime will be maximised if
4 regions of high stress are avoided. The loads on the
5 closed valve are significantly greater than loads
6 generated during valve opening. Therefore, the focus
7 should be on the closed position. Stresses are
8 highest in the region of the commissures where loads
9 are transmitted to the stent, but they are reduced
10 when the belly of the leaflet is as low as
11 practicable in the closed valve. This means that
12 there must be sufficient material in the leaflet to
13 allow the desired low closing.

14

15 SUMMARY OF THE INVENTION

16 The present invention provides a cardiac valve
17 prosthesis comprising a frame and two or more
18 leaflets (preferably three) attached to the frame.
19 Two embodiments of the invention are disclosed.

20 1. First Embodiment

21 The leaflets are attached to the frame between
22 posts, with a free edge which can seal the leaflets
23 together when the valve is closed under back
24 pressure. The leaflets are created in a
25 mathematically defined shape allowing good wash-out
26 of the whole leaflet orifice, including the area
27 close to the frame posts, thereby relieving the
28 problem of thrombus deposition under clinical implant
29 conditions.

30 The leaflet shape has a second design feature,
31 by which the pressure required to open the valve and

1 the pressure gradient across the valve in the open
2 position is reduced by creating a valve which is
3 partially open in its stable unstressed position.
4 Moulding the leaflets in a partially open position
5 permits them to open easily to a wider angle
6 resulting in an increased effective orifice area, for
7 any given polyurethane/elastomeric material. This
8 permits the use of materials from a wider range of
9 mechanical properties to fabricate the leaflets,
10 including those of a relatively stiff nature, and
11 also permits lower modulus materials to be
12 incorporated as thicker and hence more durable
13 leaflets, while retaining acceptable leaflet
14 hydrodynamic function.

15 A third design feature is the reduction of a
16 stress concentration in the vicinity of the
17 commissural region of the leaflets. In many valve
18 designs, there exists a region of localised high
19 bending where the opening part of the flexible
20 leaflet merges into the stationary region of the
21 leaflet adjacent to the valve frame. The current
22 design reduces the bending, and hence the local
23 stress concentration, in this region. This feature is
24 designed to enhance the valve durability.

25 The wide opening of the leaflet coaptation close
26 to the stent posts improves blood washout, reduces
27 thrombogenesis and minimises embolic risks to the
28 recipient, by allowing a clear channel for blood flow
29 throughout the whole valve orifice.

30 The partially open design acts to reduce the
31 fluid pressure required to open the valve. This in

1 turn results in lower pressure gradients across the
2 valve, allowing the use of durable, stiffer
3 polyurethanes to fabricate the valve which may be
4 better equipped to deal with a cyclic stress
5 application or thicker leaflets of lower modulus
6 polyurethanes, hence achieving good durability with
7 good hydrodynamic function. The position of the
8 leaflet in its stable unstressed state acts to reduce
9 the stress concentration resulting from leaflet
10 bending, hence increasing valve durability.

11 In one aspect the invention is a cardiac valve
12 prosthesis comprising a frame defining a blood flow
13 axis and at least two leaflets attached to the frame.
14 The at least two leaflets are configured to be
15 movable from an open to a closed position. The
16 leaflets have a blood inlet side and a blood outlet
17 side and are in the closed position when fluid
18 pressure is applied to the outlet side, and in the
19 open position when fluid pressure is applied to the
20 inlet side. The leaflets are in a neutral position
21 intermediate the open and closed position in the
22 absence of fluid pressure being applied to the
23 leaflets. The at least two leaflets include a first
24 leaflet. The first leaflet has a surface contour
25 such that an intersection of the first leaflet with
26 at least one plane perpendicular to the blood flow
27 axis forms a first composite wave. The first
28 composite wave is substantially defined by a first
29 wave combined with at least a second wave
30 superimposed over the first wave. The first wave has
31 a first frequency and the second wave has a second

1 frequency, different from the first frequency.
2 Alternatively, the first composite wave may be
3 defined by a first wave combined with second and
4 third waves superimposed over the first wave. The
5 third wave has a third frequency which is different
6 from the first frequency.

7 Both the first wave and the second wave may be
8 symmetric or asymmetric about a plane parallel to and
9 intersecting the blood flow axis and bisecting the
10 first leaflet. The first composite wave may be
11 symmetric or asymmetric about a plane parallel to and
12 intersecting the blood flow axis and bisecting the
13 first leaflet. The at least two leaflets may include
14 second and third leaflets. An intersection of the
15 second and third leaflets with a plane perpendicular
16 to the blood flow axis forms second and third
17 composite waves. The second and third composite
18 waves are substantially the same as the first
19 composite wave. The first and second waves may be
20 defined by an equation which is trigonometric,
21 elliptical, hyperbolic, parabolic, circular, a smooth
22 analytic function or a table of values. The at least
23 two leaflets may be configured such that they are
24 substantially free of bending stresses when in the
25 neutral position. The frame may be substantially
26 cylindrical having first and second ends, one of the
27 ends defining at least two scalloped edge portions
28 separated by at least two posts, each post having a
29 tip, and wherein each leaflet has a fixed edge joined
30 to a respective scalloped edge portion of the frame
31 and a free edge extending substantially between the

1 tips of two posts. The first and second waves may be
2 symmetric about a plane parallel to and intersecting
3 the blood flow axis and bisecting the first leaflet
4 or at least one of the first and second waves may be
5 symmetric about such plane. The first leaflet may
6 have a surface contour such that when the first
7 leaflet is in the neutral position an intersection of
8 the first leaflet with a plane parallel to and
9 intersecting the blood flow axis and bisecting the
10 first leaflet forms a fourth wave.

11 In another aspect the invention is a method of
12 making a cardiac valve prosthesis. The valve
13 prosthesis includes a frame defining a blood flow
14 axis substantially parallel to the flow of blood
15 through the valve prosthesis and at least two
16 flexible leaflets attached to the frame. The method
17 includes providing a forming element having at least
18 two leaflet forming surfaces. The forming element is
19 engaged with the frame. A coating is applied over
20 the frame and engaged forming element. The coating
21 binds to the frame. The coating over the leaflet
22 forming surfaces forms the at least two leaflets.
23 The at least two leaflets are configured to be
24 movable from an open to a closed position. The
25 leaflets have a blood inlet side and a blood outlet
26 side and are in the closed position when fluid
27 pressure is applied to the outlet side, and in the
28 open position when fluid pressure is applied to the
29 inlet side. The leaflets are in a neutral position
30 intermediate the open and closed position in the
31 absence of fluid pressure being applied to the

1 leaflets. The at least two leaflets include a first
2 leaflet. The first leaflet has a surface contour
3 such that the intersection of the first leaflet with
4 at least one plane perpendicular to the blood flow
5 axis forms a first composite wave. The first
6 composite wave is substantially defined by a first
7 wave combined with a second superimposed wave. The
8 first wave has a first frequency and the second wave
9 has a second frequency different from the first
10 frequency. After the coating is applied the forming
11 element is disengaged from the frame. The first
12 composite wave formed in the coating step may be
13 defined by a first wave combined with second and
14 third waves superimposed over the first wave. The
15 third wave has a third frequency which is different
16 from the first frequency.

17 The first and second waves formed in the coating
18 step may be either symmetric or asymmetric about a
19 plane parallel to and intersecting the blood flow
20 axis and bisecting the first leaflet. The first
21 composite wave formed in the coating step may be
22 symmetric or asymmetric about a plane parallel to and
23 intersecting the blood flow axis and bisecting the
24 first leaflet. The at least two leaflets formed in
25 the coating step may include second and third
26 leaflets. An intersection of the second and third
27 leaflets with a plane perpendicular to the blood flow
28 axis forms second and third composite waves,
29 respectively. The second and third composite waves
30 are substantially the same as the first composite
31 wave. The first and second waves formed in the

1 coating step may be defined by an equation which is
2 trigonometric, elliptical, hyperbolic, parabolic,
3 circular, a smooth analytic function or a table of
4 values.

5 The first and second waves in the coating step
6 may be symmetric about a plane parallel to and
7 intersecting the blood flow axis and bisecting the
8 first leaflet or at least one of the first and second
9 waves may be asymmetric about such plane. The at
10 least two leaflets in the coating step are configured
11 such that they are substantially free of bending
12 stresses when in the neutral position.

13 In a further aspect the invention is a cardiac
14 valve prosthesis comprising a frame defining a blood
15 flow axis and at least two leaflets attached to the
16 frame including a first leaflet. The first leaflet
17 has an internal surface facing the blood flow axis
18 and an external surface facing away from the blood
19 flow axis. The first leaflet is configured such that
20 a mean thickness of a first half of the first leaflet
21 is different than a mean thickness of a second half
22 of the first leaflet. The first and second halves
23 are defined by a plane parallel to and intersecting
24 the blood flow axis and bisecting the first leaflet.
25 The first leaflet may be further configured such that
26 a thickness of the first leaflet between the internal
27 and external surfaces along a cross section defined
28 by the intersection of a plane perpendicular to the
29 blood flow axis and the first leaflet changes
30 gradually and substantially continuously from a first

1 end of the cross section to a second end of the cross
2 section.

3 In another aspect the invention is a method of
4 making a cardiac valve prosthesis which includes a
5 frame defining a blood flow axis substantially
6 parallel to the flow of blood through the valve
7 prosthesis and at least two flexible leaflets
8 attached to the frame. The method includes providing
9 a mould having a cavity sized to accommodate the
10 frame, inserting the frame into the mould, inserting
11 the mould into an injection moulding machine, and
12 injecting molten polymer into the cavity of the mould
13 to form the at least two leaflets. The injection of
14 the molten polymer causes the at least two leaflets
15 to bond to the frame. The cavity is shaped to form
16 the at least two leaflets in a desired configuration.
17 The at least two leaflets are configured to be
18 movable from an open to a closed position. The
19 leaflets have a blood inlet side and a blood outlet
20 side and are in the closed position when fluid
21 pressure is applied to the outlet side, and in the
22 open position when fluid pressure is applied to the
23 inlet side. The leaflets are in a neutral position
24 intermediate the open and closed position in the
25 absence of fluid pressure being applied to the
26 leaflets. The at least two leaflets include a first
27 leaflet having a surface contour such that when the
28 first leaflet is in the neutral position an
29 intersection of the first leaflet with at least one
30 plane perpendicular to the blood flow axis forms a
31 first composite wave. The first composite wave is

1 substantially defined by a first wave combined with
2 at least a second superimposed wave. The first wave
3 may have a first frequency, the second wave may have
4 a second frequency, the first frequency being
5 different from the second frequency.

6 In a still further aspect the invention is a
7 method of designing a cardiac valve prosthesis which
8 includes a frame and at least two flexible leaflets
9 attached to the frame. The method includes defining
10 a first desired shape of the leaflets in a first
11 position, defining a second desired shape of the
12 leaflets in a second position different from the
13 first position, and conducting a draping analysis to
14 identify values of adjustable parameters defining at
15 least one of the first and second shapes. The
16 draping analysis ensures that the leaflets are
17 comprised of a sufficient amount and distribution of
18 material for the leaflets to assume both the first
19 and second desired shapes. Either of the first and
20 second positions in the defining steps may be a
21 closed position and the other of the first and second
22 positions may be a partially open position.

23 2. Second Embodiment

24 In one aspect, this invention is a cardiac valve
25 prosthesis comprising a substantially cylindrical
26 frame defining a blood flow axis, the frame having
27 first and second ends, one of the ends defining at
28 least two scalloped edge positions separated by at
29 least two posts, each post having a tip; and at least
30 two flexible leaflets attached to the frame, the at
31 least two leaflets being configured to be movable

1 from an open to a closed position, the at least two
2 leaflets having a blood inlet side and a blood outlet
3 side, the at least two leaflets being in the closed
4 position when fluid pressure is applied to the outlet
5 side, being in the open position when fluid pressure
6 is applied to the inlet side and being in a neutral
7 position intermediate the open and closed position,
8 in the absence of fluid pressure being applied to the
9 leaflets, each leaflet having a fixed edge joined to
10 a respective scalloped edge portion of the frame and
11 a free edge extending substantially between the tips
12 of two posts. The at least two leaflets may include
13 a first leaflet having a surface contour such that
14 when the first leaflet is in the neutral position an
15 intersection of the first leaflet with at least one
16 plane perpendicular to the blood flow axis forms a
17 first composite wave, the first composite wave being
18 substantially defined by a first wave combined with
19 at least a second wave superimposed over the first
20 wave, the first wave having a first frequency, the
21 second wave having a second frequency different than
22 the first frequency, the first wave comprising a
23 circular arc.

24 The first composite wave may be defined by a
25 first wave combined with second and third waves
26 superimposed over the first wave, the third wave
27 having a third frequency which is different from the
28 first and second frequencies. The first composite
29 wave as well as the second wave may be symmetric or
30 asymmetric about a plane parallel to and intersecting
31 the blood flow axis and bisecting the first leaflet.

1 The at least two leaflets may further include second
2 and third leaflets; and an intersection of the second
3 and third leaflets with the plane perpendicular to
4 the blood flow axis may form second and third
5 composite waves, respectively, the second and third
6 composite waves being substantially the same as the
7 first composite wave. The second wave may be defined
8 by an equation which is one of trigonometric,
9 elliptical, hyperbolic, a smooth analytic function
10 and a table of values. The at least two leaflets may
11 be configured such that they are substantially free
12 of bending stresses when in the neutral position.
13 The first leaflet may have a surface contour such
14 that when the first leaflet is in the neutral
15 position an intersection of the first leaflet with a
16 plane parallel to and intersecting the blood flow
17 axis and bisecting the first leaflet forms a fourth
18 wave.

19 In a second aspect, this invention is a method
20 of making a cardiac valve prosthesis which includes a
21 substantially cylindrical frame defining a blood flow
22 axis substantially parallel to the flow of blood
23 through the valve prosthesis and at least two
24 flexible leaflets attached to the frame, the method
25 comprising forming at least two scalloped edge
26 portions on the frame, the shape of each scalloped
27 edge portion being defined by the intersection of the
28 frame with a plane inclined with respect to the blood
29 flow axis; treating the frame to raise its surface
30 energy to above about 64mN/m; providing a forming
31 element having at least two leaflet forming surfaces;

1 engaging the forming element to the frame; applying a
2 coating over the frame and engaged forming element,
3 the coating binding to the frame, the coating over
4 the leaflet forming surfaces forming the at least two
5 flexible leaflets, the at least two leaflets being
6 configured to be movable from an open to a closed
7 position, the at least two leaflets having a blood
8 inlet side and a blood outlet side, the at least two
9 leaflets being in the closed position when fluid
10 pressure is applied to the outlet side, being in the
11 open position when fluid pressure is applied to the
12 inlet side and being in a neutral position
13 intermediate the open and closed position, in the
14 absence of fluid pressure being applied to the
15 leaflets, the at least two leaflets including a first
16 leaflet having a surface contour such that when the
17 first leaflet is in the neutral position an
18 intersection of the first leaflet with at least one
19 plane perpendicular to the blood flow axis forms a
20 first composite wave, the first composite wave being
21 substantially defined by a first wave combined with
22 at least a second superimposed wave, the first wave
23 having a first frequency, the second wave having a
24 second frequency, the first frequency being different
25 from the second frequency, the first wave comprising
26 a circular arc; and disengaging the forming element
27 from the frame.
28

1 DESCRIPTION OF DRAWINGS

2 FIG. 1 is a diagrammatic view comparing the
3 shape of symmetric (solid line) and asymmetric
4 (dashed line) leaflets.

5 FIG. 2 is a perspective view of the valve
6 prosthesis in the neutral or partially open position.

7 FIG. 3 is a sectional view similar to the
8 sectional view along line 3-3 of FIG. 2 except that
9 FIG. 3 illustrates that view when the leaflets are in
10 the closed position and illustrates the function
11 which is used to define the shape of the closed
12 leaflet belly $X_{closed}(Z)$.

13 FIG. 4A is a front view of the valve leaflet
14 shown in FIG. 2. FIG. 4B is in the same view as FIG.
15 4A and is a partial schematic view of the same closed
16 valve leaflet shown in FIG. 3 and illustrates that
17 $S(X, Y)_n$ and $S(X, Y)_{n-1}$ are contours enclosing the
18 leaflet between the function $X_{closed}(Z)$ and the scallop
19 geometry.

20 FIG. 5 is a plot of an underlying function used
21 in defining the valve leaflet in the moulded leaflet
22 partially open position P for valves made in
23 accordance with the first embodiment.

24 FIG. 6 is a plot of a symmetrical superimposed
25 function used in defining the shape of the valve
26 leaflet of the first embodiment in the moulded
27 leaflet position P .

28 FIG. 7 is a plot of the composite function used
29 in construction of the moulded leaflet position P
30 resulting from combining an underlying function (FIG.

1 5) and a symmetric superimposed function (FIG. 6) for
2 valves made in accordance with the first embodiment.

3 FIG. 8 is a plot of an asymmetric superimposed
4 function used in the construction of the moulded
5 leaflet position P for valves made in accordance with
6 the first embodiment.

7 FIG. 9 is a plot of the composite function
8 resulting from combining an underlying function
9 (FIG. 5) and an asymmetric function (FIG. 8) for
10 valves made in accordance with the first embodiment.

11 FIG. 10 is a sectional view of the valve
12 leaflets in the neutral position along line 3-3 in
13 FIG. 2 and illustrates the function which is used to
14 define the shape of the moulded leaflet belly
15 $X_{open}(Z)$.

16 FIG. 11A is a front view of the valve. FIG. 11B
17 is a partial schematic view of the valve leaflets of
18 FIG. 11A and illustrates that $P(X, Y)_n$ and $P(X, Y)_{n-1}$
19 are contours enclosing the leaflet between the
20 function $X_{open}(Z)$ and the scallop geometry.

21 FIG. 12 is a perspective view of a valve of the
22 first embodiment having symmetric leaflets.

23 FIG. 13 is a perspective view of a valve of the
24 first embodiment having asymmetric leaflets.

25 FIG. 14 is a side view of a former used in the
26 manufacture of the valve of the present invention.

27 FIG. 15 is a plot of an underlying function used
28 in defining the valve leaflet in the moulded
29 partially open position P for a valve made in
30 accordance with the second embodiment.

1 FIG. 16 is a plot of an asymmetrical
2 superimposed function used in defining the shape of a
3 valve leaflet of the second embodiment in the moulded
4 leaflet position *P* for valves made in accordance with
5 the second embodiment.

6 FIG. 17 is a plot of the composite function used
7 in construction of the moulded leaflet position *P*
8 resulting from combining an underlying function (FIG.
9 15) and an asymmetric superimposed function (FIG. 16)
10 for a valve made in accordance with the second
11 embodiment.

12 FIG. 18 is a perspective view of a valve of the
13 second embodiment having asymmetric leaflets.

14

15 DESCRIPTION OF THE INVENTION

16

17 a. Design Considerations

18 Consideration of the factors discussed above
19 results in the identification of certain design goals
20 which are achieved by the prosthetic heart valve of
21 the present invention. First, the prosthetic heart
22 valve must have enough material in the leaflet for
23 wide opening and low closing, but more than this
24 amount increases the energy barrier to opening. To
25 ensure that there is sufficient, but not an excess of
26 material, a draping analysis discussed in more detail
27 below is used. Second, to ensure sufficient material
28 for wide opening and low closing, the valve can only
29 be manufactured in a partially open position: (a) by
30 deforming the stent posts outwards during
31 manufacture; (b) by introducing multiple curves in

1 the leaflet free edge (but see below); (c) by making
2 the closed position asymmetric; and (d) combinations
3 of the above. Third, if there is enough material for
4 low closing and wide opening, the energy barrier to
5 opening may be high enough to prevent opening of all
6 leaflets at low flow. The energy barrier can be
7 minimised by: (a) introducing multiple curves in the
8 leaflet; (b) making the leaflet asymmetric; and
9 combinations of the above. Fourth, open commissures
10 are needed for blood handling and closed commissures
11 are needed for regurgitation, so the valve should
12 have partially open commissures. In particular the
13 included angle between adjacent leaflet free edges at
14 the valve commissures (for example see angle α of the
15 symmetric leaflets shown in FIG. 1) should be in the
16 range of 10-55°, preferably in the range 25-55°.

17 As discussed above, the use of multiple curves
18 in the leaflet helps assure wide opening and more
19 complete closure of the valve and to minimise the
20 energy barrier to opening of the valve. However, the
21 introduction of multiple curves of more than 1.5
22 wavelengths to the leaflet can be a disadvantage.
23 While there may be sufficient material in the leaflet
24 to allow full opening, in order for this to happen,
25 the bends in the leaflet must straighten out
26 completely. The energy available to do this arises
27 only from the pressure gradient across the open
28 valve, which decreases as the leaflets becomes more
29 open, i.e. as the valve orifice area increases. This
30 energy is relatively small (the more successful the
31 valve design the smaller it becomes), and does not

1 provide enough energy to remove leaflet curves of
2 more than 1.5 wavelengths given the stiffness of the
3 materials available for valve manufacture. The result
4 is they do not straighten out and the valve does not
5 open fully.

6 A draping analysis is used as a first
7 approximation to full finite element analysis to
8 determine if the starting shape of a membrane is such
9 that it will take on a desired final shape when
10 placed in its final position. From a durability
11 standpoint the focus is on the closed position, and
12 the desired shape of the leaflet in its closed
13 position is defined. Draping analysis allows the
14 leaflet to be reformed in a partially open position.

15 Draping analysis assumes that very low energy
16 deformation is possible (in reality any form of
17 deformation requires energy). In order for this to
18 occur the bending stiffness of the leaflet/membrane
19 must be small, each element of the membrane should be
20 free to deform relative to its neighbour, and each
21 element should be free to change shape, i.e. the
22 shear modulus of the material is assumed to be very
23 low. In applying the draping analysis, it is assumed
24 that the leaflet can be moved readily from an
25 original defined closed position to a new position in
26 which it is manufactured. When the valve is actually
27 cycled, it is assumed that the leaflet when closing
28 will move from the manufactured position to the
29 originally defined closed position. This allows the
30 closed position to be optimized from a stress
31 distribution aspect, and the manufactured position to

1 be optimized from the point of view of reducing the
2 energy barrier to opening.

3 Both symmetric and asymmetric shapes of the
4 leaflet can allow incorporation of sufficient
5 material in the leaflet free edge to allow full
6 opening. FIG. 1 is a diagrammatic view comparing the
7 shape of symmetric (solid line) and asymmetric
8 (dashed line) leaflets and also showing the
9 commissure area 12 where the leaflets connect to the
10 frame. An advantage of the asymmetric shape is that
11 a region of higher radius of curvature 14 is produced
12 than is achieved with a symmetric curve having a
13 lower radius of curvature 16. This region can buckle
14 more readily and thereby the energy barrier to
15 opening is reduced.

16 An asymmetric leaflet also reduces the energy
17 barrier through producing unstable buckling in the
18 leaflet. During opening symmetric leaflets buckle
19 symmetrically i.e. the leaflet buckles are generally
20 mirrored about the centerline of the leaflet thus
21 balancing the bending energies about this centerline.
22 In the asymmetric valve the region of higher radius
23 buckles readily, and because these bending energies
24 are not balanced about the center line, this buckle
25 proceeds to roll through the leaflet producing a
26 sail-like motion producing a low energy path to open.

27 An additional feature of the asymmetric valve is
28 that the open position is also slightly asymmetric,
29 as a result of which it offers a somewhat helical
30 flow path, and this can be matched to the natural
31 helical sense of the aorta. Suggested benefits of

1 this helical flow path include reduction of shear
2 stress non-uniformity at the wall, and consequent
3 reduction of platelet activation.

4

5 b. The Valve Prosthesis

6 First and second embodiments of the valve
7 prosthesis will be described with reference to the
8 accompanying drawings. FIG. 2 is a perspective view
9 of a heart valve prosthesis made in accordance with
10 the present invention. The valve 10 comprises a
11 stent or frame 1 and attached leaflets 2a, 2b, and
12 2c. The leaflets are joined to the frame at scallops
13 5a, 5b, and 5c. Between each scallop is post 8, the
14 most down-stream part of which is known as a stent
15 tip 6. Leaflets 2a, 2b, and 2c have free edges 3a,
16 3b, and 3c, respectively. The areas between the
17 leaflets at the stent tips 6 form commissures 4.

18 1. First embodiment of heart valve prosthesis

19 The following describes a particular way of
20 designing a first embodiment of a valve of the
21 present invention. Other different design methodology
22 could be utilized to design a valve having the
23 structural features of the valve disclosed herein.
24 Five computational steps are involved in this
25 particular method:

- 26 (1) Define the scallop geometry (the scallop, 5,
27 is the intersection of the leaflet, 2, with
28 the frame, 1);
29 (2) Geometrically define a valve leaflet in the
30 closed position C;

- 1 (3) Map and compute the distribution of area
- 2 across the leaflet in the closed position;
- 3 (4) Rebuild the leaflet in a partially open
- 4 position *P*; and
- 5 (5) Match the computed leaflet area distribution
- 6 in the partially open or moulded position *P*
- 7 to the defined leaflet in the closed position
- 8 *C*. This ensures that when an increasing
- 9 closing pressure is applied to the leaflets,
- 10 they eventually assume a shape which is
- 11 equivalent to that defined in closed position
- 12 *C*.

13 This approach allows the closed shape of the
14 leaflets in position *C* to be optimised for durability
15 while the leaflets shaped in the moulded partially
16 open shape *P* can be optimised for haemodynamics. This
17 allows the use of stiffer leaflet materials for
18 valves which have good haemodynamics. An XYZ co-
19 ordinate system is defined as shown in FIG. 2, with
20 the Z axis in the flow direction of blood flowing
21 through the valve.

22 The leaflets are mounted on the frame, the shape
23 of which results from the intersection of the
24 aforementioned leaflet shape and a 3-dimensional
25 geometry that can be cylindrical, conical or
26 spherical in nature. A scallop shape is defined
27 through intersecting the surface enclosed by the
28 following equations with a cylinder of radius *R*
29 (where *R* is the internal radius of the valve):

$$X_{el} = E_{s0} - E_{sJ} \sqrt{1 - \left(\frac{Z}{E_{sN}} \right)^2}$$

$$H_{sJ} = E_{s0} - E_{sJ} \sqrt{1 - \left(\frac{Z}{E_{sN}} \right)^2} - H_{s0}$$

$$H_{sN}(Z) = H_{sJ} \cdot \tan(60) \cdot f(Z)$$

- 1 where $f(Z)$ is a function changing with Z .

$$X_{hyp} = H_{s0} + H_{sJ} \sqrt{1 - \left(\frac{Y}{H_{sN}} \right)^2}$$

- 1 The shape of the scallop can be varied using the
 2 constants E_{s0} , E_{sJ} , H_{s0} , $f(Z)$. The definition of
 3 parameters used in these and the other equations
 4 herein are contained in Table 4.
- 5 The shape of the leaflet under back pressure
 6 (i.e. in the closed position C) can be approximated
 7 mathematically using elliptical or hyperbolic co-
 8 ordinates, or a combination of the above in an XYZ
 9 co-ordinate system where XY is the plane of the valve
 10 perpendicular to the blood flow and Z is the
 11 direction parallel to the blood flow. The parameters
 12 are chosen to define approximately the shape of the
 13 leaflet under back pressure so as to allow convenient
 14 leaflet re-opening and minimise the effect of the
 15 stress component which acts in the direction parallel
 16 to the blood flow, whilst also producing an effective
 17 seal under back pressure.
- 18 The closed leaflet geometry in closed position C
 19 is chosen to minimise stress concentrations in the
 20 leaflet particularly prone to occur at the valve

1 commissures. The specifications for this shape
2 include:

- 3 (1) inclusion of sufficient material to allow a
4 large open-leaflet orifice;
- 5 (2) arrangement of this material to minimise
6 redundancy (excess material in the free edge,
7 3) and twisting in the centre of the free
8 edge, 3; and
- 9 (3) arrangement of this material to ensure the
10 free edge, 3, is under low stress i.e.
11 compelling the frame and leaflet belly to
12 sustain the back-pressure.

13 FIG. 3 is a partial sectional view (using the
14 section 3-3 shown in FIG. 2) showing only the
15 intended position of the leaflet in the closed
16 position. The shape of this intended position is
17 represented by the function $X_{closed}(Z)$. This function
18 can be used to arrange the shape of the leaflet in
19 the closed position C to meet the aforementioned
20 specification. The curve is defined using the
21 following equation and manipulated using the
22 constants E_{cJ} , E_{cO} , Z_{cO} and the functions $E_{cN}(Z)$ and
23 $X_T(Z)$.

$$24 \quad X_{closed}(Z) = - \left[E_{cJ} \left(1 - \left(\frac{Z - Z_{cO}}{E_{cN}(Z)} \right)^2 \right) \right]^{0.5} + E_{cO} - X_T(Z)$$

25

26 where E_{cN} is a function changing linearly with Z and
27 $X_T(Z)$ is a function changing nonlinearly with Z.

28

1 Thus the scallop shape and the function $X_{closed}(Z)$
2 are used to form the prominent boundaries for the
3 closed leaflet in the closed position C. The
4 remaining part of the leaflet is formed using
5 contours $S(X, Y)_n$ sweeping from the scallop to the
6 closed leaflet belly function $X_{closed}(Z)$, where n is an
7 infinite number of contours, two of which are shown
8 in FIG. 4B.

9 The length of the leaflet (or contours $S(X, Y)_n$)
10 in the circumferential direction (XY) is calculated
11 and repeated in the radial direction (Z) yielding a
12 function $L(Z)$ which is used later in the definition
13 of the geometry in the partially open position P. The
14 area contained between respective contours is also
15 computed yielding a function $K(Z)$ which is also used
16 in the definition of the geometry in position P. The
17 area contained between contours is approximated using
18 the process of triangulation as shown in FIG. 4B.
19 This entire process can be shortened by reducing the
20 number of contours used to represent the surface
21 ($100 < n < 200$).

22 The aforementioned processes essentially define
23 the leaflet shape and can be manipulated to optimise
24 for durability. In order to optimise for
25 haemodynamics, the same leaflet is moulded in a
26 position P which is intermediate in terms of valve
27 opening. This entails moulding large radius curves
28 into the leaflet which then serve to reduce the
29 energy required to buckle the leaflet from the closed
30 to the open position. The large radius curves can be

1 arranged in many different ways. Some of these are
2 outlined herein.

3 The leaflet may be moulded on a dipping former
4 as shown in FIG. 14. Preferably the former is tapered
5 with an included angle θ so that the end 29 has a
6 diameter which is greater than the end 22. (This
7 ensures apposition of the frame and former during
8 manufacture.). In this case, the scallop shape,
9 defined earlier, is redefined to lie on a tapered
10 geometry (as opposed to the cylindrical geometry used
11 in the definition of the closed leaflet shape). This
12 is achieved by moving each point on the scallop
13 radially, and in the same movement, rotation of each
14 point about an X-Y plane coincident with the bottom
15 of the scallop, until each point lies on the tapered
16 geometry.

17 The geometry of the leaflet shape can be defined
18 as a trigonometric arrangement (or other mathematical
19 function) preferably sinusoidal in nature in the XY
20 plane, comprising one or more waves, and having
21 anchoring points on the frame. Thus the valve
22 leaflets are defined by combining at least two
23 mathematical functions to produce composite waves,
24 and by using these waves to enclose the leaflet
25 surface with the aforementioned scallop.

26 One such possible manifestation is a composite
27 curve consisting of an underlying low frequency
28 sinusoidal wave upon which a second higher frequency
29 sinusoidal wave is superimposed. A third wave having
30 a frequency different from the first and second waves
31 could also be superimposed over the resulting

1 composite wave. This ensures a wider angle between
2 adjacent leaflets in the region of the commissures
3 when the valve is fully open thus ensuring good wash-
4 out of this region.

5 The composite curve, and the resulting leaflet,
6 can be either symmetric or asymmetric about a plane
7 parallel to the blood flow direction and bisecting a
8 line drawn between two stent tips such as, for
9 leaflet 2a, the section along line 3-3 of FIG. 2.
10 The asymmetry can be effected either by combining a
11 symmetric underlying curve with an asymmetric
12 superimposed curve or *vice versa*.

13 The following describes the use of a symmetric
14 underlying function with an asymmetric superimposed
15 function, but the use of an asymmetric underlying
16 function will be obvious to one skilled in the art.
17 The underlying function is defined in the XY plane
18 and connects the leaflet attachment points to the
19 scallop at a given height from the base of the valve.
20 This underlying function shown in FIG. 5, can be
21 trigonometric, elliptical, hyperbolic, parabolic,
22 circular, or other smooth analytic function or could
23 be a table of values.

24 Using sine functions, one possible underlying
25 wave is shown in FIG. 5 and is defined using the
26 following equation.

$$X_u = X_{(n,0)} + A_u \cdot \sin \left[\left(\frac{0.5\pi}{Y_{(n,0)}} \right) (Y - Y_{(n,0)}) \right]$$

1 The superimposed wave is defined in the XY
2 plane, and connects the attachment points of the
3 leaflet to the scallop at a given height above the
4 base of the valve. The superimposed wave is of higher
5 frequency than the underlying wave, and can be
6 trigonometric, elliptic, hyperbolic, parabolic,
7 circular, or other smooth analytic function, or a
8 table of values.

9 Using sine functions, one possible symmetric
10 leaflet design is formed when the underlying wave is
11 combined with a superimposed wave formed using the
12 following equation.

13

14
$$X_s = -A_s B_s(Y) \sin \left[\left(\frac{1.5\pi}{Y_{(n,0)}} \right) (Y - Y_{(n,0)}) \right]$$

15

16 A_s can be varied across the leaflet to produce
17 varying wave amplitude across the leaflet, for
18 example lower amplitude at the commissures than in
19 the leaflet centre. B_s can be varied to adjust the
20 length of the wave. The superimposed wave is shown
21 in FIG. 6. The composite wave formed by combining
22 the underlying wave (FIG. 5) with the superimposed
23 wave (FIG. 6) is shown in FIG. 7.

24 Using sine functions, one possible asymmetric
25 leaflet design is formed when the underlying wave
26 (FIG. 5) is combined with a superimposed wave formed
27 using the following equation.

$$X_s = -A_s \cdot B_s(Y) \cdot \sin \left[\left(\frac{\pi}{Y_{(n,0)}} \right) (Y - Y_{(n,0)}) \right]_{0}^{Y_{(n,0)}}$$

$$X_s = 0.5 \cdot A_s \cdot B_s(Y) \cdot \sin \left[\left(\frac{2.0\pi}{Y_{(n,0)}} \right) Y \right]_{(-Y_{(n,0)})}^0$$

1 A_s can be varied across the leaflet to produce
 2 varying wave amplitude across the leaflet, for
 3 example lower amplitude at the commissures than in
 4 the leaflet centre. $B_s(Y)$ can be varied to adjust the
 5 length of the wave. The superimposed wave is shown
 6 in FIG. 8. The resulting asymmetric composite wave
 7 is shown in FIG. 9. The composite wave $W(X_c, Y_c)_n$ is
 8 created by offsetting the superimposed wave normal to
 9 the surface of the underlying wave (FIGS. 7, 9).

10 While the general shape of the leaflet in
 11 position P has been determined using the composite
 12 wave, at this stage it is not specified in any
 13 particular position. In order to specify the position
 14 of P , the shape of the partially open leaflet
 15 position can be defined as $X_{open}(Z)$. This is shown as
 16 reference numeral 7 in FIG. 10.

17 One possible function determining this shape is
 18 given as follows:

19

$$20 \quad X_{open}(Z) = - \left[E_{\omega} \left(1 - \left(\frac{Z - Z_{\omega O}}{E_{\omega N}} \right)^2 \right) \right]^{0.5} + E_{\omega O}$$

21

22 In order to manipulate the composite wave to
 23 produce the belly shape $X_{open}(Z)$ the respective

1 amplitudes of the individual sine waves can be varied
2 from the free edge to the leaflet base. For example,
3 the degree of 'openness' of the leaflet in position P
4 can be varied throughout the leaflet.

5 The composite wave is thus defined to produce
6 the moulded "buckle" in the leaflet, and $X_{open}(Z)$ is
7 used to define the geometry of the leaflet at
8 position P . At this stage it may bear no relation to
9 the closed leaflet shape in position C . In order to
10 match the area distribution of both leaflet
11 positions, (thus producing essentially the same
12 leaflet in different positions) the composite wave
13 length is iterated to match the length of the
14 relevant leaflet contour in position C . Thus the
15 amplitude and frequency of the individual waves can
16 be varied in such a manner as to balance between: (a)
17 producing a resultant wave the length of which is
18 equal to the relevant value in the length function
19 $L(Z)$ thus approximating the required closed shape
20 when back pressure is applied, and (b) allowing
21 efficient orifice washout and ready leaflet opening.
22 Also the area contained between the contours in the
23 open leaflet is measured using the same process of
24 triangulation as in the closed position C , and is
25 iterated until it matches with the area contained
26 between relevant contours in position C (denoted
27 $K(Z)$) (through tilting the contours in P relative to
28 each other). Thus the composite waves $(P(X, Y)_n)$
29 pertaining to the contour n and length $L(Z)$ can be
30 tilted at an angle to the XY plane about attachment
31 points $X_{(n,0)}$, $Y_{(n,0)}$ and $X_{(n,0)}$, $-Y_{(n,0)}$ until the correct

1 area is contained between $P(X,Y)_n$ and $P(X,Y)_{n-1}$ (See
2 FIGS. 10 & 11).

3 This process identifies the values of B_s , A_u and
4 the contour tilt angle to be used in constructing the
5 mould for the valve leaflet. As long as the constants
6 such as B_s and A_u , and the tilt angle of the contours
7 relative to the XY plane, are known, the surface of
8 the leaflet in its moulded position can be
9 visualised, enclosed and machined in a conventional
10 manner. As a result of this fitting process the
11 composite wave retains the same basic form but
12 changes in detail from the top of the leaflet to the
13 bottom of the leaflet. A composite wave can be
14 defined in the leaflet surface as the intersection of
15 the leaflet surface with a plane normal to the Z
16 axis. This composite wave will have the same general
17 form as the composite wave used in the leaflet design
18 but will differ from it in detail as a result of the
19 tilting process described above.

20 In summary therefore one possible method of
21 designing the leaflet of the first embodiment of the
22 present invention is in the following way:

- 23 (1) Define a scallop shape;
- 24 (2) Define a shape approximating the shape of the
25 closed leaflet using elliptical, hyperbolic,
26 parabolic or circular functions, smooth
27 analytical functions or table of values;
- 28 (3) Compute the functions $L(Z)$ and $K(Z)$, which
29 define the length of the leaflet in the XY
30 plane along the Z axis and the area
31 distribution of the leaflet along the Z axis;

- 1 (4) Use one or more associated sine waves to
2 generate a geometry which is partially-open,
3 which pertains to a leaflet position which is
4 between the two extreme conditions of normal
5 valve function, i.e. leaflet open and leaflet
6 closed;
- 7 (5) Vary the frequency and amplitude of the
8 sinewaves to fit to the length function $L(Z)$
9 and the angle at which the contour is tilted
10 to the XY plane to fit to the area function
11 $K(Z)$; and
- 12 (6) The respective amplitudes of the individual
13 sine waves can be varied from the free edge
14 to leaflet base, for example the degree of
15 'openness' of the leaflet can be varied
16 throughout the leaflet.

17 Examples 1 and 2 set forth hereafter are
18 examples of how the invention of the first embodiment
19 can be put into practice. Using the scallop constants
20 in Table 1, the constants required to produce an
21 example of a symmetric leaflet valve (example 1, FIG.
22 12) and an example of an asymmetric leaflet valve
23 (example 2, FIG. 13) are given in Table 2 and Table 3
24 respectively. These constants are used in conjunction
25 with the aforementioned equations to define the
26 leaflet geometry.

27 With one leaflet described using the
28 aforementioned equations, the remaining two leaflets
29 are generated by rotating the geometry about the Z
30 axis through 120° and then through 240° . These
31 leaflet shapes are inserted as the leaflet forming

1 surfaces of the dipping mould (otherwise known as a
2 dipping former), which then forms a 3-dimensional
3 dipping mould. The composite wave described in the
4 aforementioned equations, therefore substantially
5 defines the former surface which produces the inner
6 leaflet surface.

7 As seen in FIG. 14 the dipping mould 20 is
8 slightly tapered so that the end 29 has a diameter
9 which is greater than the end 22, and has a first end
10 22 having an outside diameter slightly smaller than
11 the inside diameter of the frame. The former
12 includes at least two and preferably three leaflet
13 forming surfaces 24 which are defined by scalloped
14 edges 26 and flats 28. Sharp edges in the
15 manufacturing former and on the frame are radiused to
16 help reduce stress concentrations in the finished
17 valve. During the dip moulding process the frame is
18 inserted over end 22 of the former so that the
19 scallops 5 and stent posts 8 of the frame align with
20 the scalloped edges 26 and flats 28 of the former.
21 The leaflet forming surfaces 24 are configured to
22 form leaflets during the moulding process which have
23 the geometry described herein. This mould can be
24 manufactured by various methods, such as, machining,
25 electrical discharge machining, injection moulding.
26 In order that blood flow is not disturbed, a high
27 surface finish on the dipping mould is essential.

28 For the frame there are preferably three posts
29 with leaflets hung on the frame between the posts. A
30 crown-like frame or stent, 1, is manufactured with a
31 scallop geometry, which matches the dipping mould

1 scallop. The frame scallop is offset radially by
2 0.1mm to allow for the entire frame to be coated with
3 a thin layer of leaflet material to aid adhesion of
4 the leaflets. Leaflets may be added to the frame by a
5 dip-moulding process, using a dipping former machined
6 or moulded to create the multiple sinewave form.

7 The material of preference for the frame should
8 be a semi-rigid fatigue- and creep-resistant frame
9 material such as polyetheretherketone (PEEK), high
10 modulus polyurethane, titanium, reinforced
11 polyurethane, or polyacetal (Delrin) produced by
12 machining or injection-moulding etc. The frame can
13 be machined or injection moulded, and is manufactured
14 preferably from PEEK or polyacetal (Delrin).

15 Alternatively, the frame material may comprise a
16 relatively low modulus polymer, which may be fabric-
17 reinforced or fiber-reinforced to more closely mimic
18 the aortic wall. Such a valve would be a synthetic
19 equivalent of a freestyle tissue valve. Rather than
20 having a rigid frame to which a sewing ring is
21 subsequently attached such a valve would incorporate
22 a fabric at the leaflet margin through which the
23 surgeon sutures to attach the valve in place. The
24 leaflet and scallop geometry of such a valve are
25 designed in exactly the same way as for a rigidly
26 stented valve. The low modulus polymer which is
27 incorporated in the fabric is preferably the same
28 polymer from which the valve leaflets are made and is
29 incorporated into the fabric during the dipping or
30 moulding process for the valve leaflets.

1 The frame is treated by exposure to a gas plasma
2 or other methods to raise its surface energy above 64
3 mN/m (milliNewtons/meter) Then the frame is
4 dipped in a polyurethane solution (preferably Elast-
5 EonTM manufactured by Aortech Biomaterials Pty,
6 Sydney Australia) in order to apply a coating of
7 approximately 0.1mm thick. Having dried the frame
8 with applied coating in an oven overnight, it is
9 placed on the dipping former and aligned with the
10 former scallops. The combination of frame and three
11 dimensional dipping mould is then dipped into
12 polyurethane solution, which forms a coating of
13 solution on frame and mould. This coating flows
14 slowly over the entire mould surface ensuring a
15 smooth coating. The new coating on the frame and
16 dipping mould solvates the initial frame coating thus
17 ensuring a good bond between leaflet and frame. The
18 dipping mould with polyurethane covering is dried in
19 an oven until all the solvent has been removed. One
20 or more dips may be used to achieve a leaflet with a
21 mean thickness between 40µm and 500µm. The shape of
22 the former, and the viscosity and solvent interactive
23 properties of the polyurethane solution, control the
24 leaflet thickness and the distribution of thickness
25 over the leaflet. A dipping process does not allow
26 precise control of leaflet thickness and its
27 variation across a leaflet. In particular, surfaces
28 that are convex on the dipping former result in
29 reduced leaflet thickness when compared with surfaces
30 that are concave. Additionally the region of the
31 leaflet adjacent to the frame essentially provides a

1 very small concave radius which traps further polymer
2 solution and this results in thickening of these
3 regions.

4 The shape of the former is substantially defined
5 by the composite wave. Radiusing and polishing of
6 the former can both contribute to some variation of
7 the shape. The shape of the inner surface of the
8 leaflets will closely replicate the shape of the
9 former. The shape of the outer surface of the
10 leaflets will be similar to the shape of the inner
11 surface but variations will result from the
12 processing properties of the polymer solution and
13 details of the dipping process used to produce the
14 valve. The leaflet may be formed from polyurethanes
15 having a Young's modulus less than 100MPa, preferably
16 in the range 5 to 50 MPa.

17 The valve is next removed from the dipping
18 mould. The stent posts, which had been deflected by
19 the taper on the former, now recover their original
20 position. The shape of the leaflets changes slightly
21 as a result of the movement of the stent posts.

22 At this stage the dipping mould and frame is
23 covered with an excess of polyurethane due to the
24 drain-off of the polymer onto the region of the mould
25 known as the drain-off area 30. Leaflet free edges
26 may be trimmed of excess material using a sharp blade
27 rotated around the opened leaflets or using laser-
28 cutting technology.

29 An alternate valve manufacturing method is
30 injection moulding. A mould is constructed with a
31 cavity which allows the valve frame to be inserted in

1 the mould. The cavity is also designed with the
2 leaflet geometry, as defined above, as the inner
3 leaflet surface. A desired thickness distribution is
4 defined for the leaflet and the outer leaflet surface
5 of the mould is constructed by adding the leaflet
6 thickness normally to the inner leaflet surface. The
7 leaflet may be of uniform thickness throughout, in
8 the range 40 to 500 microns, preferably 50 to 200
9 microns, more preferably 80 to 150 microns. The
10 leaflet may be thickened towards its attachment to
11 the frame. Alternatively the thickness of the
12 leaflet, along a cross-section defined by the
13 intersection of a plane perpendicular to the blood
14 flow axis and the leaflet, can change gradually and
15 substantially continuously from a first end of the
16 cross-section (i.e. first edge of the leaflet) to a
17 second end of the cross-section (i.e. second edge of
18 the leaflet) in such a way that the mean thickness of
19 the first half of the leaflet is different from the
20 mean thickness of the second half of the leaflet.
21 This mould is inserted in a conventional injection
22 moulding machine, the frame is inserted in the mould
23 and the machine injects molten polymer into the
24 cavity to form the leaflets and bond them to the
25 frame. The polymer solidifies on cooling and the
26 mould is opened to allow the complete valve to be
27 removed.

28 The leaflets may also be formed using a
29 reaction-moulding process (RIM) whereby the polymer
30 is synthesised during the leaflet forming. A mould is
31 constructed as described above. This mould is

1 inserted in a reaction-injection moulding machine,
2 the frame is inserted in the mould and the machine
3 injects a reactive mixture into the cavity. The
4 polymer is produced by the reaction in the cavity to
5 form the leaflets and bond them to the frame. When
6 the reaction is complete, the mould is opened to
7 allow the complete valve to be removed.

8 Yet a further option is to compression mould a
9 valve initially dipped. This approach allows the
10 leaflet thickness or thickness distribution to be
11 adjusted from that initially produced. By varying
12 the thickness of the leaflets the dynamics of the
13 valve opening and closing can be modified. For
14 example, the thickness of the leaflet along a cross-
15 section defined by the intersection of a plane
16 perpendicular to the blood flow axis and the leaflet
17 can be varied so that the thickness changes gradually
18 and substantially continuously from a first end of
19 the cross-section (i.e. first edge of the leaflet) to
20 a second end of the cross-section (i.e. second edge
21 of the leaflet) in such a way that the mean thickness
22 of the first half of the leaflet is different from
23 the mean thickness of the second half of the leaflet.
24 This will result in the thinner half of the leaflet
25 opening first and creating a sail-like opening motion
26 along the free edge of the leaflet.

27 Leaflet shape resulting from conventional
28 injection moulding, reaction injection moulding or
29 compression moulding, is substantially defined by the
30 composite wave described above. It will differ in

1 detail for many of the same reasons identified for
2 dip moulding.

3 The valves of the present invention are
4 manufactured in the neutral position or close to it
5 and are therefore substantially free of bending
6 stresses in this position. As a result when the
7 leaflet is moved to its closed position the total
8 bending energy at the leaflet center free edge and at
9 the commissures is reduced compared to a valve made
10 according to U.S. Patent No. 5,376,113.

11 The valves of the present invention may be used
12 in any required position within the heart to control
13 blood flow in one direction, or to control flow
14 within any type of cardiac assist device.

15 The following examples 1 and 2 use the same
16 scallop geometry described using the constants set
17 forth in Table 1: While the examples described herein
18 relate to one valve size, the same method can be used
19 to produce valves from a wide range of sizes. This
20 can be carried out by modifying the constants used in
21 the equations, by rescaling the bounding curves such
22 as $X_{closed}(Z)$ and computing and iterating in the normal
23 fashion or by rescaling the leaflet.

24
25

	values (mm)
R	11.0
E_{So}	21.7
E_{BJ}	21.5
E_{SN}	13.8

H_{so}	0.18
$f(Z)$	$(0.05.Z)+1.0$

1

2

Table 1

3

Example 1.

4

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The parameters described in the preceding sections are assigned the values set forth in Table 2 and are used to manufacture a symmetric valve. The included angle between adjacent leaflet free edges at the valve commissure for this valve is approximately 50°.

Parameter	Value (mm)
<i>Closed position</i>	
Z_{co}	0
Z_{co}	0.0
$E_{cn}(Z)$	$E_{cn}=3.0.Z+50.3$
E_{co}	22.0
E_{cn}	20.0
$X_T(Z)$	0.0
<i>Partially-open position</i>	
θ	12.7°
E_{cn}	50.0
Z_{co}	4.0
E_{co}	51.8
E_{cn}	27.7
A_u	Result from iteration procedure finds that A_u varies from 1e-5 at the leaflet base to 5.1 at 4mm from the leaflet base to 3.8 at the free edge.
$A_s(Y)$	1.0

B_s	Result from iteration procedure finds that B_s varies from $1e-3$ at the leaflet base to 1.6 at $3mm$ from the leaflet base to 0.6 at the free edge.
-------	--

Table 2

1 FIG. 12 shows the symmetric valve which is
 2 manufactured, using the values outlined in Table 1
 3 and Table 2.

4

5 Example 2

6 The parameters described in the preceding
 7 sections are assigned the values set forth in Table 3
 8 and are used to manufacture an asymmetric valve. The
 9 included angle between adjacent leaflet free edges at
 10 the valve commissure for this valve is approximately
 11 48° .

Parameter	Value (mm)
<i>Closed position</i>	
Z_{co}	0.0
$E_{cn}(Z)$	$E_{cn}=3.0 \cdot Z+48.9$
E_{co}	18.4
E_{coj}	20.0
$X_{T(Z)}$	$X_{T(n-1)}=0.97 \cdot (X_{T(n)})$ where $X_{T(\text{free edge})}=2.1$
<i>Partially-open position</i>	
θ	7.1°
E_{oj}	50.0
Z_{oo}	5.0

E_{oo}	51.5
E_{on}	29.0
A_u	Result from iteration procedure finds that A_u varies from $1e-5$ at the leaflet base to 3.1 at 3mm from the leaflet base to 2.2 at 9mm from the leaflet base to 3.8 at the free edge.
$B_s(Y)$	$B_s(Y) = (Y-c)/m$ where $B_s=1$ at leaflet base and $m=5.04$ and $c=-15.1$ at leaflet free edge.
B_s	Result from iteration procedure finds that B_s varies from $1e-3$ at the leaflet base to 1.1 at 6mm from the leaflet base to 0.4 at the free edge.

Table 3

- 1 FIG. 13 shows the valve which is manufactured
 2 using the values outlined in Table 1 and Table 3.
 3

Definition of parameters	
R	Internal radius of valve
Scallop (FIG. 2)	
X_{ell} , H_{SV} , H_{SN} , X_{hyp} are used to define a surface which, when intersected with a cylinder, scribe a function which forms the scallop for one leaflet. This method for creating a scallop is described in Mackay et al. Biomaterials 17 1996. although an added variable $f(Z)$ is used for added versatility.	
X_{ell}	Scribes an ellipse in the radial direction.
X_{hyp}	Scribes a hyperbola in the circumferential direction.
E_{eo}	Ellipse X-axis offset

E_{SJ}	Major axis of the ellipse
E_{BN}	Minor axis of the ellipse
H_{SJ}	Major axis of the hyperbola
H_{BN}	Minor axis of the hyperbola
H_{SO}	Hyperbola x-axis offset
$F(Z)$	Creates a varying relationship between H_{SN} and H_{SJ}
Closed Leaflet geometry C (FIGS. 3 & 4)	
$X_{closed}(Z)$ is defined as an ellipse (with a minor axis $E_{CN}(Z)$ which changes with Z) in the XZ axis in the plane defined in FIG. 2 by cutting plane 3-3. It is defined using the following constants and functions.	
Z_{CO}	Closed ellipse Z-axis offset
$E_{CN}(Z)$	Closed ellipse minor axis which changes with Z
E_{CO}	Closed ellipse X-axis offset
E_{CJ}	Closed ellipse major axis
$X_T(Z)$	Offset function which serves to increase the amount of material in the belly
Moulded position P	
P is enclosed by a number (n) of contours $P(X,Y)_n$ which run from one side of the scallop to the other. The underlying function X_u is used in defining both symmetric and asymmetric leaflets. X_u is simply an ellipse (or other such function) running in a plane from one side of the scallop to the other. The points on the scallop are designated $X_{(n,0)}$, $Y_{(n,0)}$ where n refers to the contour number (see FIGS. 5, 7, 9, 11B).	
Y	Variable in plane from $Y_{(n,0)}$ to $-Y_{(n,0)}$
A_u	A_u is the amplitude of the underlying wave
$A_s(Y)$	A_s is a function which biases the wave amplitude in a defined way, e.g. the amplitude of the wave can be increased near the commissure if so desired.

E_s	E_s is the amplitude of the superimposed wave
Composite Curve (FIGS. 7 & 9)	
X_c	X coordinate for defining the composite curve. This is derived using X_n and X_s
Y_c	Y coordinate for defining the composite curve. This is derived using X_n and X_s
Open Leaflet position (FIG. 10)	
<p>$X_{open}(Z)$ is defined as an ellipse in the XZ axis in the plane defined in FIG. 2 by cutting plane 3-3. The contours defined in Composite Curve are married to the Open Leaflet position $X_{open}(Z)$ to produce the moulded leaflet P. It is defined using the following constants.</p>	
E_{maj}	Open ellipse major axis
Z_{co}	Open ellipse Z-axis offset
E_{co}	Open ellipse X-axis offset
E_{cn}	Open ellipse minor axis
θ	Former taper angle

Table 4

1

2

1 2. Second embodiment of heart valve prosthesis

2 The following describes another particular way
3 of designing a second embodiment of a valve of the
4 present invention. Other different design methodology
5 could be utilized to design a valve having the
6 structural features of the valve disclosed herein.
7 Five computational steps are involved in this
8 particular method:

- 9 (1) Define the scallop geometry (the scallop, 5,
10 is the intersection of the leaflet, 2, with
11 the frame, 1);
- 12 (2) Define a contour length function $L(z)$ and use
13 this function to define a valve leaflet in
14 the closed position C and optimize the stress
15 distribution on the valve. The stress
16 distribution can be confirmed using Finite
17 Element Analysis (FEA). Thus the resulting
18 stress distribution results from the length
19 function $L(Z)$ and FEA is used to confirm the
20 optimal $L(Z)$.
- 21 (4) Rebuild the leaflet in a partially open
22 position P ; and
- 23 (5) Match, using contour lengths, the computed
24 leaflet area distribution in the partially
25 open or moulded position P to the defined
26 leaflet in the closed position C . This
27 ensures that when an increasing closing
28 pressure is applied to the leaflets, they
29 eventually assume a shape which is equivalent
30 to that defined in closed position C .
- 31

1 This approach allows the closed shape of the
2 leaflets in position C to be optimised for durability
3 while the leaflets shaped in the moulded partially
4 open shape P can be optimised for haemodynamics. This
5 allows the use of stiffer leaflet materials for
6 valves which have good haemodynamics. An XYZ co-
7 ordinate system is defined as shown in FIG. 2, with
8 the Z axis in the flow direction of blood flowing
9 through the valve.

10 The leaflets are mounted on the frame, the shape
11 of which results from the intersection of the
12 aforementioned leaflet shape and a 3-dimensional
13 geometry that can be cylindrical, conical or
14 spherical in nature.

15 The leaflets are mounted on the frame, the shape
16 of which results from the intersection of the
17 aforementioned leaflet shape and a 3-dimensional
18 geometry that can be cylindrical, conical or
19 spherical in nature. A scallop shape is defined
20 through cutting a cylinder of radius R (where R is
21 the internal radius of the valve) with a plane at an
22 inclined angle. The angle of the cutting plane is
23 dictated by the desired height of the leaflet and the
24 desired distance between the leaflets at the
25 commissures.

26 The closed leaflet geometry in closed position C
27 is chosen to minimise stress concentrations in the
28 leaflet particularly prone to occur at the valve
29 commissures. The specifications for this shape
30 include:

- 1 (1) inclusion of sufficient material to allow a
- 2 large open-leaflet orifice;
- 3 (2) arrangement of this material to minimise
- 4 redundancy (excess material in the free edge,
- 5 3) and twisting in the centre of the free
- 6 edge, 3; and
- 7 (3) arrangement of this material to ensure the
- 8 free edge, 3, is under low stress i.e.
- 9 compelling the frame and leaflet belly to
- 10 sustain the back-pressure.

11

12 The closed leaflet geometry is formed using

13 contours $S(X, Y)_n$ sweeping from attachment points on

14 one side of the scallop to the congruent attachment

15 point on the opposite side of the scallop, where n is

16 an infinite number of contours, two of which are

17 shown in FIG. 4B. The geometry of the contours $S(X,$

18 $Y)_n$ can be simple circular arcs or a collection of

19 circular arcs and tangential lines; the length of

20 each contour is defined by $L(Z)$. Hence the geometry

21 is defined and modified using the length function

22 $L(Z)$.

23 Thus the scallop shape and the contours $S(X, Y)_n$

24 are used to form the prominent boundaries for the

25 closed leaflet in the closed position C. This process

26 can be shortened by reducing the number of contours

27 used to represent the surface ($5 < n < 200$). For design

28 iteration, the ease with which the leaflet shape can

29 be changed can be improved by reducing the number of

30 contours to a minimum (i.e. $n=5$), although the

31 smoothness of the resulting leaflet could be

1 compromised to some extent. Upon optimising the
2 function $L(Z)$ for stress distribution, the number of
3 contours defining the leaflet can be increased to
4 improve the smoothness of the resulting leaflet (100
5 $< n < 200$). The function $L(Z)$ is used later in the
6 definition of the geometry in the partially open
7 position P .

8 The aforementioned processes essentially define
9 the leaflet shape and can be manipulated to optimise
10 for durability. In order to optimise for
11 haemodynamics, the same leaflet is moulded in a
12 position P which is intermediate in terms of valve
13 opening. This entails moulding large radius curves
14 into the leaflet which then serve to reduce the
15 energy required to buckle the leaflet from the closed
16 to the open position. The large radius curves can be
17 arranged in many different ways. Some of these are
18 outlined herein.

19 As previously described with respect to the
20 first embodiment the leaflet may be moulded on a
21 dipping former as shown in FIG. 14. However, in this
22 embodiment to aid removal of the valve from the
23 former and reduce manufacturing stresses in the
24 leaflet the former is preferably not tapered.

25 The geometry of the leaflet shape can be defined
26 as a circular and trigonometric arrangement (or other
27 mathematical function) preferably circular and
28 sinusoidal in nature in the XY plane, comprising one
29 or more waves, and having anchoring points on the
30 frame. Thus the valve leaflets are defined by
31 combining at least two mathematical functions to

1 produce composite waves, and by using these waves to
2 enclose the leaflet surface with the aforementioned
3 scallop.

4 One such possible manifestation is a composite
5 curve consisting of an underlying circular arc or
6 wave upon which a second higher frequency sinusoidal
7 wave is superimposed. A third wave having a frequency
8 different from the first and second waves could also
9 be superimposed over the resulting composite wave.
10 This ensures a wider angle between adjacent leaflets
11 in the region of the commissures when the valve is
12 fully open thus ensuring good wash-out of this
13 region.

14 The composite curve, and the resulting leaflet,
15 can be either symmetric or asymmetric about a plane
16 parallel to the blood flow direction and bisecting a
17 line drawn between two stent tips such as, for
18 leaflet 2a, the section along line 3-3 of FIG. 2.
19 The asymmetry can be effected either by combining a
20 symmetric underlying curve with an asymmetric
21 superimposed curve or vice versa, or by utilising a
22 changing wave amplitude across the leaflet.

23 The following describes the use of a symmetric
24 underlying function with an asymmetric superimposed
25 function, but the use of an asymmetric underlying
26 function will be obvious to one skilled in the art.
27 The underlying function is defined in the XY plane
28 and connects the leaflet attachment points to the
29 scallop at a given height from the base of the valve.
30 This underlying function shown in FIG. 15, can be
31 trigonometric, elliptical, hyperbolic, parabolic,

1 circular, or other smooth analytic function or could
2 be a table of values.
3 The superimposed wave is defined in the XY plane, and
4 connects the attachment points of the leaflet to the
5 scallop at a given height above the base of the
6 valve. The superimposed wave is of higher frequency
7 than the underlying wave, and can be trigonometric,
8 elliptic, hyperbolic, parabolic, circular, or other
9 smooth analytic function, or a table of values.
10 One possible asymmetric leaflet design is formed when
11 the underlying wave formed using a circular arc is
12 combined with a superimposed wave formed using the
13 following equation.

14
15
16
$$X_s = -A_s B_s(Y) \sin \left[\left(\frac{1.5\pi}{Y_{(n,0)}} \right) (Y - Y_{(n,0)}) \right]$$

17
18
19 A circular arc is defined by its cord length,
20 $2Y_{(n,0)}$, and amplitude, A_s , as shown in FIG. 15. A_s
21 can be varied across the leaflet to produce varying
22 wave amplitude across the leaflet, for example lower
23 amplitude in one commissure than the opposite
24 commissure. B_s can be varied to adjust the length of
25 the wave. The superimposed wave is shown in FIG. 16.
26 The composite wave formed by combining the underlying
27 wave (FIG. 15) with the superimposed wave (FIG. 16)
28 is shown in FIG. 17. The composite wave $W(X_c, Y_c)_n$ is
29 created by offsetting the superimposed wave from
30 the surface of the underlying wave (FIG. 17).

1 Positive γ is defined as the direction of the normal
2 to the underlying wave relative to the x-axis. When
3 Y is positive, the composite curve is created by
4 offsetting in the direction positive γ and where Y is
5 negative the composite curve is created by offsetting
6 in the direction negative γ (the offset direction is
7 shown by arrows for a positive Y point and a negative
8 Y point in FIG. 17.

9 While the general shape of the leaflet in
10 position P has been determined using the composite
11 wave, at this stage it is not specified in any
12 particular position. In order to specify the position
13 of P , the shape of the partially open leaflet
14 position can be defined using the ratio of the
15 amplitude of the circular arc A_c to the amplitude of
16 the sinusoidal wave B_s .

17 A large ratio results in a leaflet which is
18 substantially closed and vice versa. In this example
19 the ratio changes from 10 at the base of the leaflet
20 to 4 at the free edge of the leaflet. The result of
21 this is a leaflet which effectively is more open at
22 the free edge than at the base of the leaflet. In
23 this way, the degree of 'openness' of the leaflet in
24 position P can be varied throughout the leaflet.

25 The composite wave is thus defined to produce
26 the moulded "buckle" in the leaflet, and the
27 amplitude ratio is used to define the geometry of the
28 leaflet at position P . At this stage it may bear no
29 relation to the closed leaflet shape in position C .
30 In order to match the area distribution of both
31 leaflet positions, (thus producing essentially the

1 same leaflet in different positions) the composite
2 wave length is iterated to match the length of the
3 relevant leaflet contour in position C. Thus the
4 amplitude and frequency of the individual waves can
5 be varied in such a manner as to balance between: (a)
6 producing a resultant wave the length of which is
7 equal to the relevant value in the length function
8 $L(Z)$ thus approximating the required closed shape
9 when back pressure is applied, and (b) allowing
10 efficient orifice washout and ready leaflet opening.

11 This process identifies the values of A_v and B_s
12 to be used in constructing the mould for the valve
13 leaflet. As long as the constants such as A_v and B_s
14 are known, the surface of the leaflet in its moulded
15 position can be visualised, enclosed and machined in
16 a conventional manner. As a result of this fitting
17 process the composite wave retains the same basic
18 form but changes in detail from the top of the
19 leaflet to the bottom of the leaflet. A composite
20 wave can be defined in the leaflet surface as the
21 intersection of the leaflet surface with a plane
22 normal to the Z axis.

23 In summary therefore one possible method of
24 designing the leaflet of the second embodiment of the
25 present invention is in the following way:

- 26 (1) Define a scallop shape;
- 27 (2) Define a shape representing the closed
28 leaflet using a contour length function $L(Z)$;
- 29 (3) Use circular arcs and sine waves to generate
30 a geometry which is partially-open, which
31 pertains to a leaflet position which is

1 between the two extreme conditions of normal
2 valve function, i.e. leaflet open and leaflet
3 closed;

4 (5) Vary the amplitude of the arcs and the
5 sinewaves to fit to the length function $L(Z)$;
6 and

7 (6) The respective amplitudes of the circular
8 arcs and sine waves can be varied from the
9 free edge to leaflet base, for example the
10 degree of 'openness' of the leaflet can be
11 varied throughout the leaflet.

12 Example 3 set forth hereafter is an example of
13 how the invention of the second embodiment can be put
14 into practice. Using the scallop constants in Table
15 5, the constants required to produce an example of an
16 asymmetric leaflet valve are given in Table 6. These
17 constants are used in conjunction with the
18 aforementioned equations to define the leaflet
19 geometry.

20 With one leaflet described using the
21 aforementioned equations, the remaining two leaflets
22 are generated by rotating the geometry about the Z
23 axis through 120° and then through 240° . These
24 leaflet shapes are inserted as the areas of the
25 dipping mould (otherwise known as a dipping former),
26 which form the majority of the leaflet forming
27 surfaces, and which then forms a 3-dimensional
28 dipping mould. The composite wave described in the
29 aforementioned equations, therefore substantially
30 defines the former surface which produces the inner
31 leaflet surface. A drain-off area 30 is also created

1 on the former to encourage smooth run-off of polymer
2 solution. The drain-off region 30 is defined by
3 extruding the leaflet free edge away from the leaflet
4 and parallel to the flow direction of the valve for a
5 distance of approximately 10mm. The transition from
6 leaflet forming surface of the dipping mould 24 to
7 the drain-off surface of the dipping mould 30 is
8 radiused with a radius greater than 1mm and
9 preferably greater than 2 mm to eliminate
10 discontinuities in the leaflet.

11 The details of the manufacture of the valve of
12 the second embodiment are similar to those previously
13 described with respect to the valve of the first
14 embodiment until the valve is removed from the
15 dipping mould. Since the former used in making the
16 valve of the second embodiment is not tapered the
17 stent posts are not deflected by the former and do
18 not move or change the leaflet shape when the valve
19 is removed from the mould. At this stage the dipping
20 mould and frame is covered with an excess of
21 polyurethane due to the drain-off of the polymer onto
22 the region of the mould known as the drain-off area
23 30. To maintain the integrity of the frame coating,
24 the leaflet is trimmed above the stent tips at a
25 distance of between 0.025 to 5mm preferably 0.5mm to
26 1.5mm from the stent tip. Thus part of the surface of
27 the leaflet is formed on the drain-off region 30
28 which is substantially defined using the composite
29 wave $W(X_0, Y_0)_0$. Leaflet free edges may be trimmed of
30 excess material using a sharp blade rotated around

1 the opened leaflets or using laser-cutting technology
2 or other similar technology.

3 The valve of the second embodiment may be used
4 in any required position within the heart to control
5 blood flow in one direction, or to control flow
6 within any type of cardiac assist device.

7 The following example 3 uses the same scallop
8 geometry described using the constants set forth in
9 Table 5: While the example 3 described herein relates
10 to one valve size, the same method can be used to
11 produce valves from a wide range of sizes. This can
12 be carried out by modifying the constants used in the
13 equations, and computing and iterating in the normal
14 fashion or by rescaling the leaflet.

15

16

17

18

	values (mm)
R	11.0
slope	-2.517
intersection	14.195

19

20

Table 5

21

1 Example 3.

2 The parameters described in the preceding
 3 sections are assigned the values set forth in Table 6
 4 and are used to manufacture an asymmetric valve
 5 according to the second embodiment. The included
 6 angle between adjacent leaflet free edges at the
 7 valve commissure for this valve is approximately 30°.

Parameter	Value (mm)
<i>Closed position</i>	
$L(\theta)$	Varies from 0.025mm at the leaflet base to 21.3mm at the free edge
<i>Partially-open position</i>	
θ	0°
A_u	Result from iteration procedure finds that A_u varies from 0.0006 at the leaflet base to 3.8 at 10.7mm from the leaflet base to 3.35 at the free edge.
A_s	At the free edge of the leaflet, $A_s(Y)$ varies from 1.5mm at one side of the scallop to 1.0mm at the opposite side of the scallop. At the base of the leaflet, $A_s(Y)$ is 1.0mm.
E_s	Result from iteration procedure finds that A_s varies from 0.0006 at the leaflet base to 0.839mm at the free edge.

Table 6

1 FIG. 18 shows the asymmetric valve which is
 2 manufactured, using the values outlined in Table 5
 3 and Table 6.

4
 5
 6

Definition of parameters	
R	Internal radius of valve
Scallop (Fig. 2)	
The scallop is defined using a simple straight line, defined using a slope and intersection, to cut with a cylinder.	
Closed Leaflet geometry C	
$L(Z)$ is used to modify the inherent geometry of the leaflet. Circular arcs and straight lines can be used to enclose the surface defined using $L(Z)$.	
Moulded position P	
P is enclosed by a number (n) of contours $W(X,Y)_n$ which run from one side of the scallop to the other. The underlying function is used in defining both symmetric and asymmetric leaflets. running in a plane from one side of the scallop to the other. The points on the scallop are designated $X_{(n,0)}$, $Y_{(n,0)}$ where n refers to the contour number (see Figs. 15,16,17,18).	
Y	Variable in plane from $Y_{(n,0)}$ to $-Y_{(n,0)}$
A_u	A_u is the amplitude of the underlying wave
$A_s(Y)$	A_s is a function which biases the wave amplitude in a defined way, e.g. the amplitude of the wave can be varied from commissure to commissure to produce asymmetry in the leaflet.
E_s	E_s is the amplitude of the superimposed wave

Composite Curve (Figs. 17)	
x_c	X coordinate for defining the composite curve.
y_c	Y coordinate for defining the composite curve.
Open Leaflet position (Fig. 18)	
The open leaflet position is defined using a ratio which determines the degree of "openness" of the leaflet.	
θ	Former taper angle

1

2

3

Table 7

1 What is claimed is:

2

3 1. A cardiac valve prosthesis comprising:

4 a substantially cylindrical frame defining
5 a blood flow axis, the frame having first and
6 second ends, one of the ends defining at least
7 two scalloped edge positions separated by at
8 least two posts, each post having a tip; and
9 at least two flexible leaflets attached to
10 the frame, the at least two leaflets being
11 configured to be movable from an open to a
12 closed position, the at least two leaflets
13 having a blood inlet side and a blood outlet
14 side, the at least two leaflets being in the
15 closed position when fluid pressure is applied
16 to the outlet side, being in the open position
17 when fluid pressure is applied to the inlet side
18 and being in a neutral position intermediate the
19 open and closed position, in the absence of
20 fluid pressure being applied to the leaflets,
21 each leaflet having a fixed edge joined to a
22 respective scalloped edge portion of the frame
23 and a free edge extending substantially between
24 the tips of two posts.

25

26 2. The valve prosthesis of claim 1 wherein the at
27 least two leaflets include a first leaflet having a
28 surface contour such that when the first leaflet is
29 in the neutral position an intersection of the first
30 leaflet with at least one plane perpendicular to the
31 blood flow axis forms a first composite wave, the

1 first composite wave being substantially defined by a
2 first wave combined with at least a second wave
3 superimposed over the first wave, the first wave
4 having a first frequency, the second wave having a
5 second frequency different than the first frequency,
6 the first wave comprising a circular arc.

7

8 3. The valve prosthesis of claim 2 wherein the
9 first composite wave is defined by a first wave
10 combined with second and third waves superimposed
11 over the first wave, the third wave having a third
12 frequency which is different from the first and
13 second frequencies.

14

15 4. The valve prosthesis of claim 2 wherein the
16 second wave is symmetric about a plane parallel to
17 and intersecting the blood flow axis and bisecting
18 the first leaflet.

19

20 5. The valve prosthesis of claim 2 wherein the
21 second wave is asymmetric about a plane parallel to
22 and intersecting the blood flow axis and bisecting
23 the first leaflet.

24

25 6. The valve prosthesis of claim 2 wherein the
26 first composite wave is symmetric about a plane
27 parallel to and intersecting the blood flow axis and
28 bisecting the first leaflet.

29

30 7. The valve prosthesis of claim 2 wherein the
31 first composite wave is asymmetric about a plane

1 parallel to and intersecting the blood flow axis and
2 bisecting the first leaflet.

3

4 8. The valve prosthesis of claim 2 wherein the at
5 least two leaflets further include second and third
6 leaflets and wherein an intersection of the second
7 and third leaflets with the plane perpendicular to
8 the blood flow axis forms second and third composite
9 waves, respectively, the second and third composite
10 waves being substantially the same as the first
11 composite wave.

12

13 9. The valve prosthesis of claim 2 wherein the
14 second wave is defined by an equation which is one of
15 trigonometric, elliptical, hyperbolic, a smooth
16 analytic function and a table of values.

17

18 10. The valve prosthesis of claim 1 wherein the at
19 least two leaflets are configured such that they are
20 substantially free of bending stresses when in the
21 neutral position.

22

23 11. The valve prosthesis of claim 6 wherein the
24 first and second waves are symmetric about a plane
25 parallel to and intersecting the blood flow axis and
26 bisecting the first leaflet.

27

28 12. The valve prosthesis of claim 7 wherein at least
29 one of the first and second waves is asymmetric about
30 a plane parallel to and intersecting the blood flow
31 axis and bisecting the first leaflet.

1

2 13. The valve prosthesis of claim 2 wherein the
3 first leaflet has a surface contour such that when
4 the first leaflet is in the neutral position an
5 intersection of the first leaflet with a plane
6 parallel to and intersecting the blood flow axis and
7 bisecting the first leaflet forms a fourth wave.

8

9 14. The valve prosthesis of claim 1 wherein the
10 frame comprises a low modulus polymer.

11

12 15. A method of making a cardiac valve prosthesis
13 which includes a substantially cylindrical frame
14 defining a blood flow axis substantially parallel to
15 the flow of blood through the valve prosthesis and at
16 least two flexible leaflets attached to the frame,
17 the method comprising:

18 forming at least two scalloped edge
19 portions on the frame, the shape of each
20 scalloped edge portion being defined by the
21 intersection of the frame with a plane inclined to
22 with respect to the blood flow axis;

23 treating the frame to raise its surface
24 energy to above about 64mN/m;

25 providing a forming element having at least
26 two leaflet forming surfaces;

27 engaging the forming element to the frame;

28 applying a coating over the frame and
29 engaged forming element, the coating binding to
30 the frame, the coating over the leaflet forming
31 surfaces forming the at least two flexible

1 leaflets, the at least two leaflets being
2 configured to be movable from an open to a
3 closed position, the at least two leaflets
4 having a blood inlet side and a blood outlet
5 side, the at least two leaflets being in the
6 closed position when fluid pressure is applied
7 to the outlet side, being in the open position
8 when fluid pressure is applied to the inlet side
9 and being in a neutral position intermediate the
10 open and closed position, in the absence of
11 fluid pressure being applied to the leaflets,
12 the at least two leaflets including a first
13 leaflet having a surface contour such that when
14 the first leaflet is in the neutral position an
15 intersection of the first leaflet with at least
16 one plane perpendicular to the blood flow axis
17 forms a first composite wave, the first
18 composite wave being substantially defined by a
19 first wave combined with at least a second
20 superimposed wave, the first wave having a first
21 frequency, the second wave having a second
22 frequency, the first frequency being different
23 from the second frequency, the first wave
24 comprising a circular arc; and
25 disengaging the forming element from the
26 frame.

27
28 16. The method of claim 15 wherein the first
29 composite wave formed in the coating step is defined
30 by a first wave combined with second and third waves
31 superimposed over the first wave, the third wave

1 having a third frequency which is different from the
2 first frequency.

3

4 17. The method of claim 15 wherein the second wave
5 formed in the coating step is symmetric about a plane
6 parallel to and intersecting the blood flow axis and
7 bisecting the first leaflet.

8

9 18. The method of claim 15 wherein the second wave
10 formed in the coating step is asymmetric about a
11 plane parallel to and intersecting the blood flow
12 axis and bisecting the first leaflet.

13

14 19. The method of claim 15 wherein the first
15 composite wave formed in the coating step is
16 symmetric about a plane parallel to and intersecting
17 the blood flow axis and bisecting the first leaflet.

18

19 20. The method of claim 15 wherein the first
20 composite wave formed in the coating step is
21 asymmetric about a plane parallel to and intersecting
22 the blood flow axis and bisecting the first leaflet.

23

24 21. The method of claim 15 wherein the at least two
25 leaflets formed in the coating step include second
26 and third leaflets and wherein an intersection of the
27 second and third leaflets with the plane
28 perpendicular to the blood flow axis forms second and
29 third composite waves, respectively, the second and
30 third composite waves being substantially the same as
31 the first composite wave.

1

2 22. The method of claim 15 wherein the second wave
3 formed in the coating step is defined by an equation
4 which is one of trigonometric, elliptical,
5 hyperbolic, a smooth analytic function and a table of
6 values.

7

8 23. The method of claim 19 wherein the first and
9 second waves formed in the coating step are symmetric
10 about a plane parallel to and intersecting the blood
11 flow axis and bisecting the first leaflet.

12

13 24. The method of claim 20 wherein at least one of
14 the first and second waves formed in the coating step
15 is asymmetric about a plane parallel to and
16 intersecting the blood flow axis and bisecting the
17 first leaflet.

18

19 25. The method of claim 15 wherein the at least two
20 leaflets formed in the coating step are configured
21 such that they are substantially free of bending
22 stresses when in the neutral position.

23

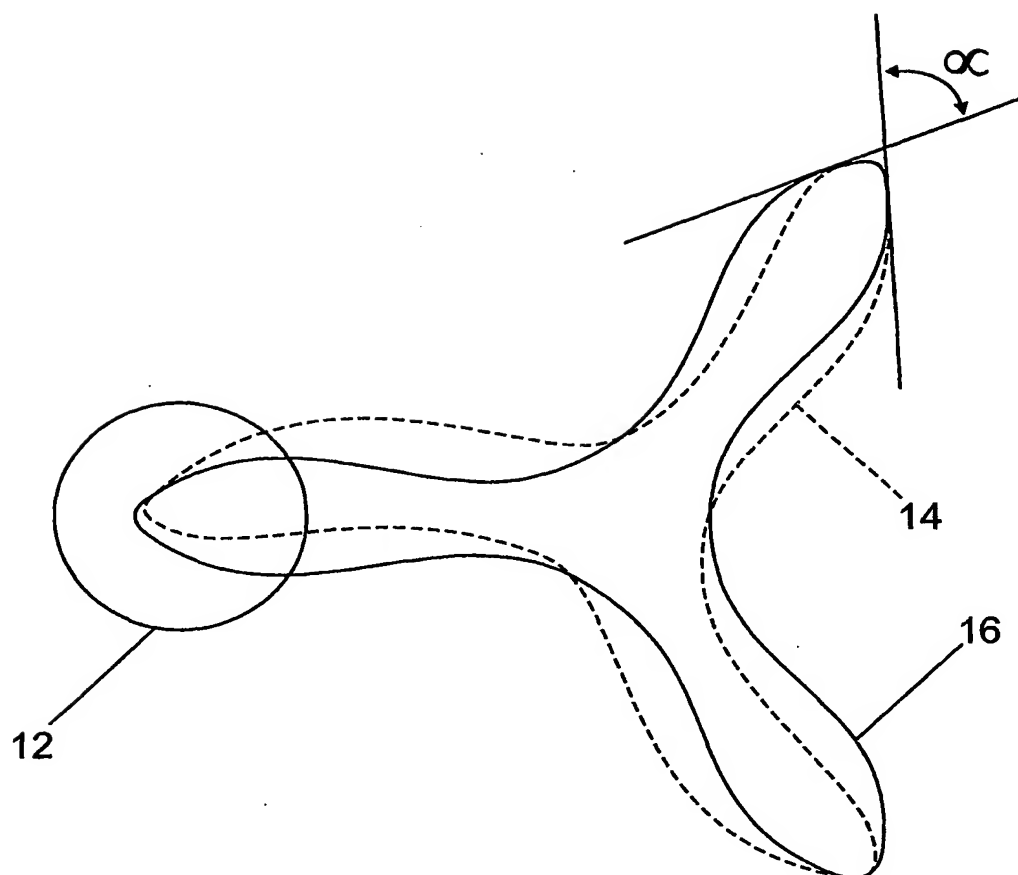


Fig. 1

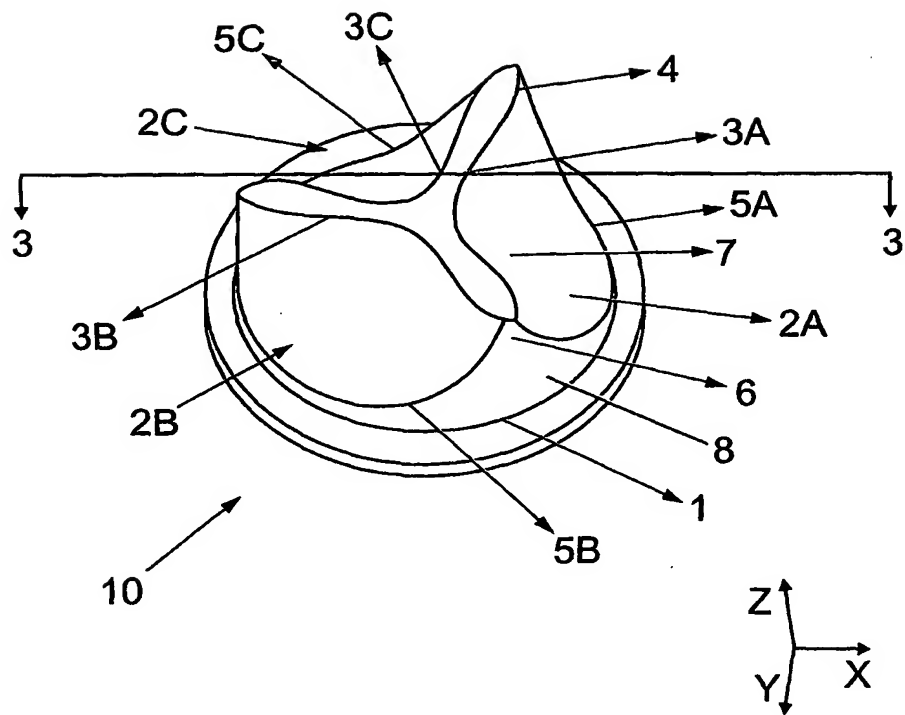


Fig. 2

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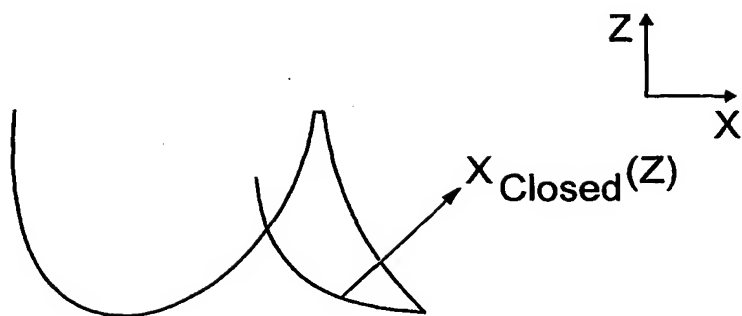


Fig. 3

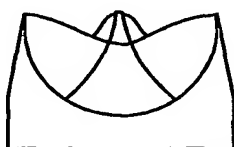


Fig. 4A

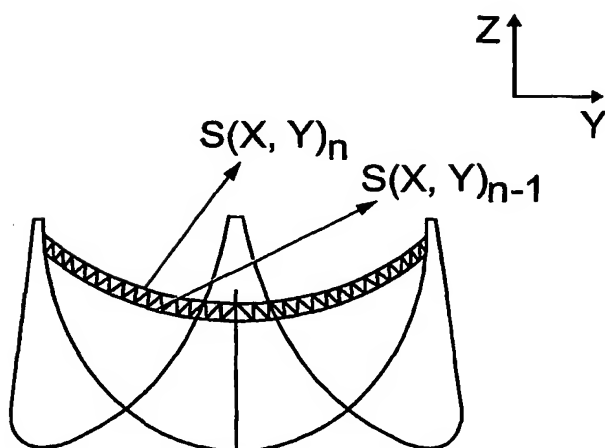
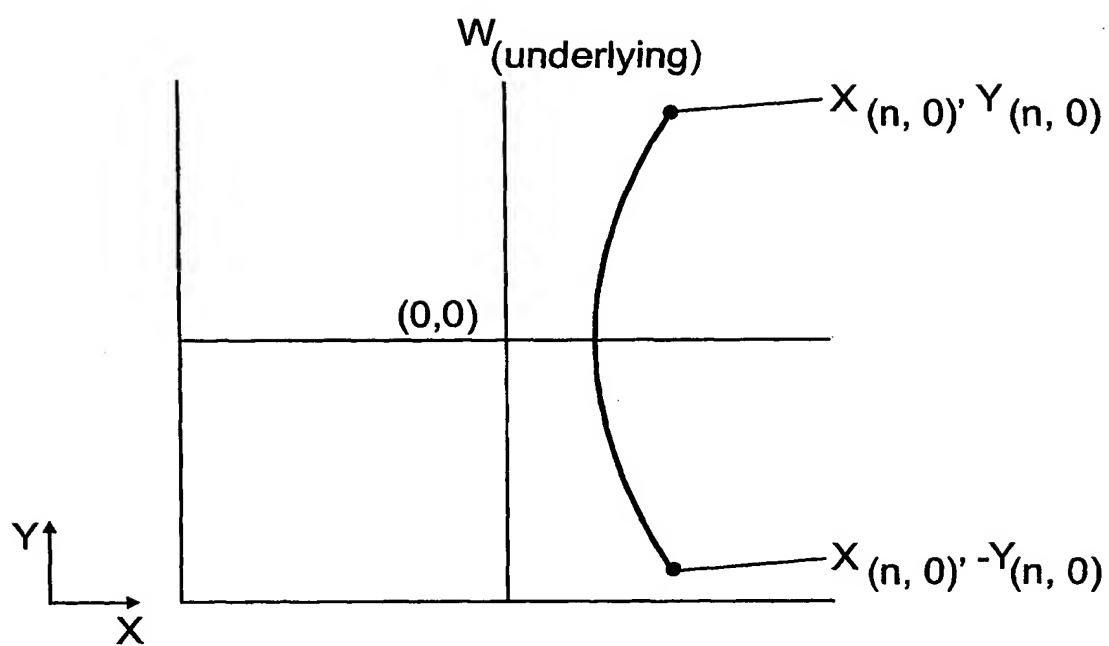


Fig. 4B

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*Fig. 5*

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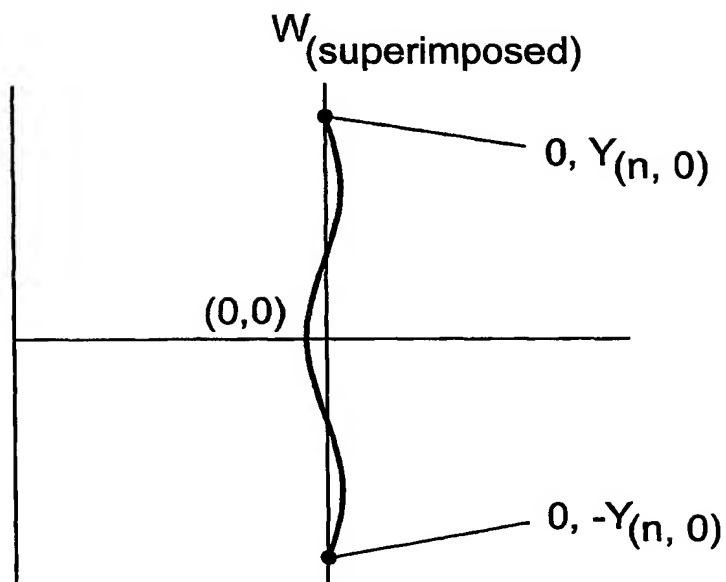


Fig. 6

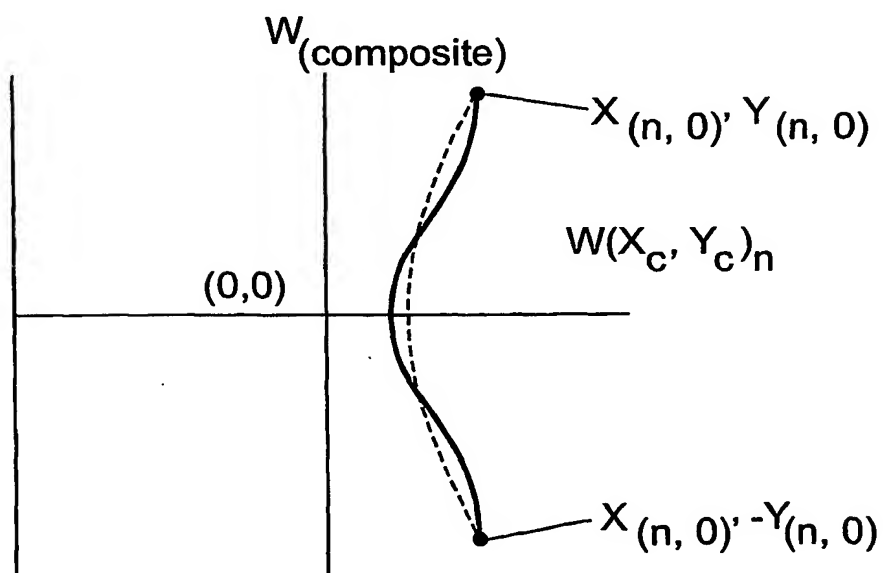


Fig. 7

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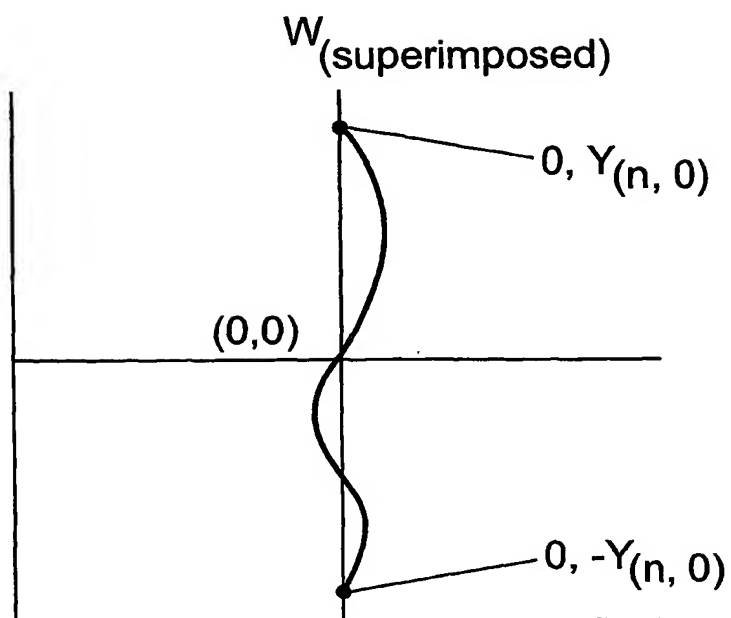


Fig. 8

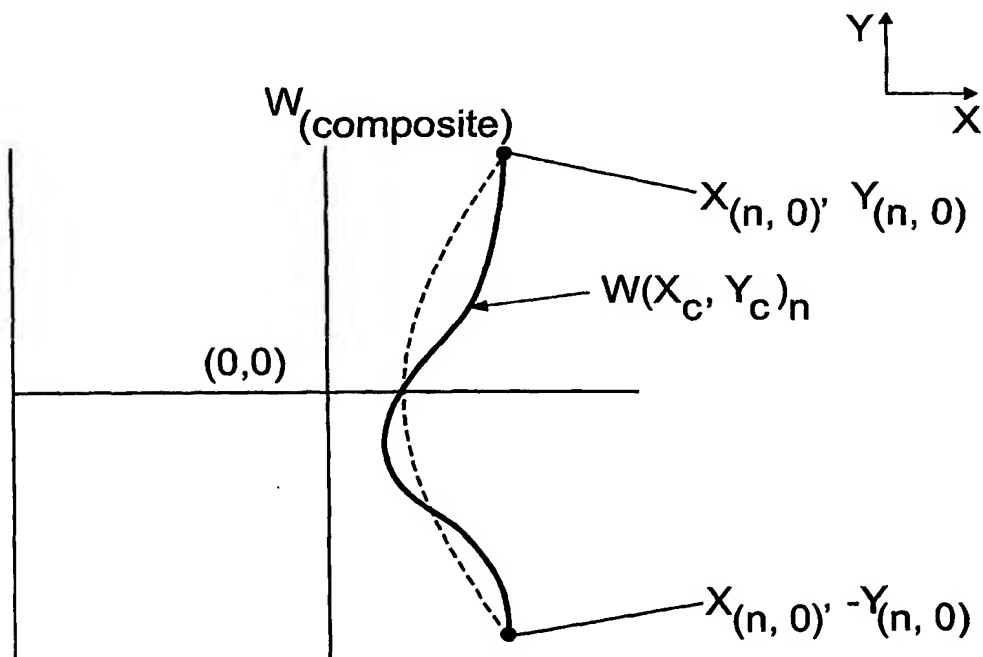


Fig. 9

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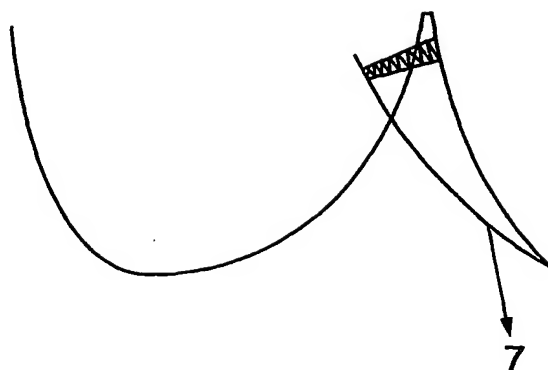


Fig. 10

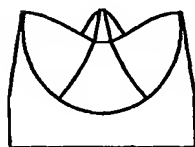


Fig. 11A

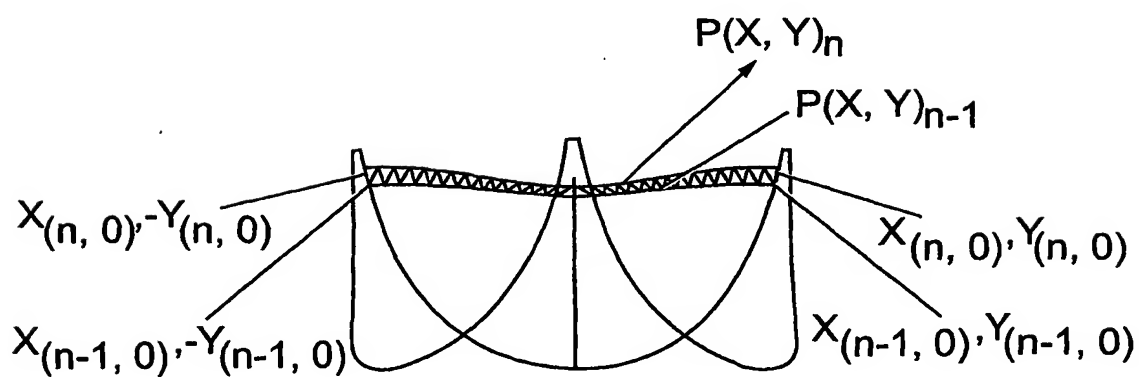


Fig. 11B

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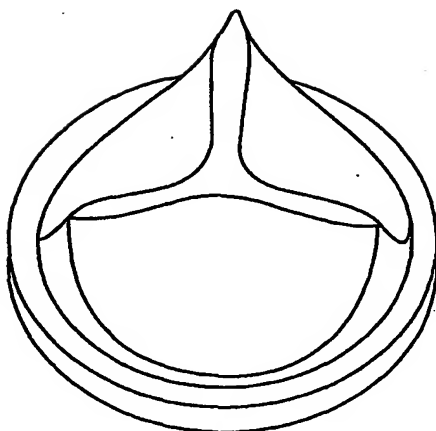


Fig. 12

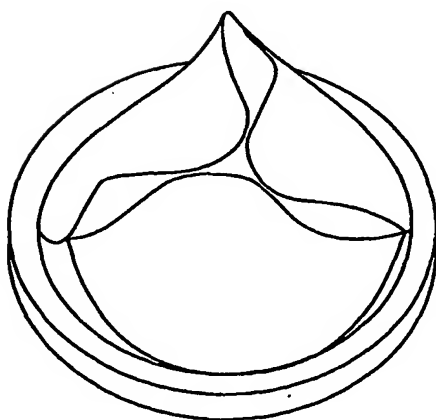


Fig. 13

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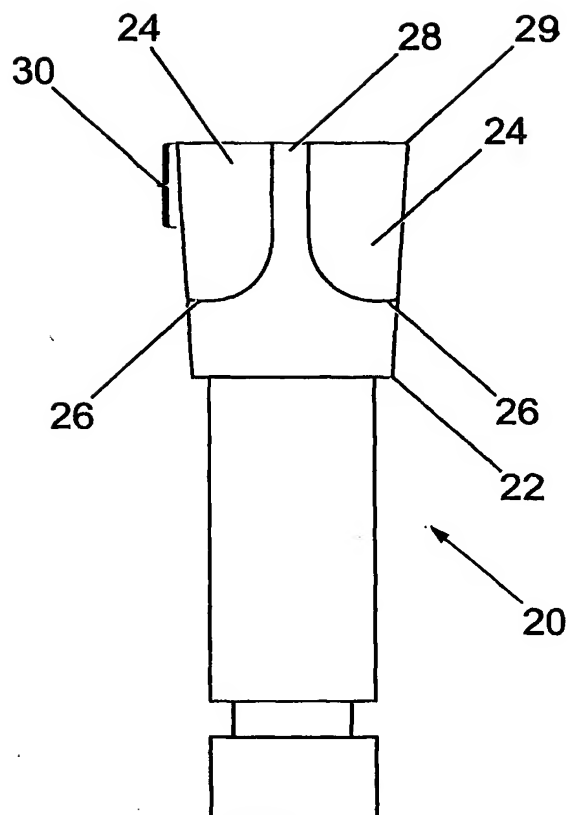


Fig. 14

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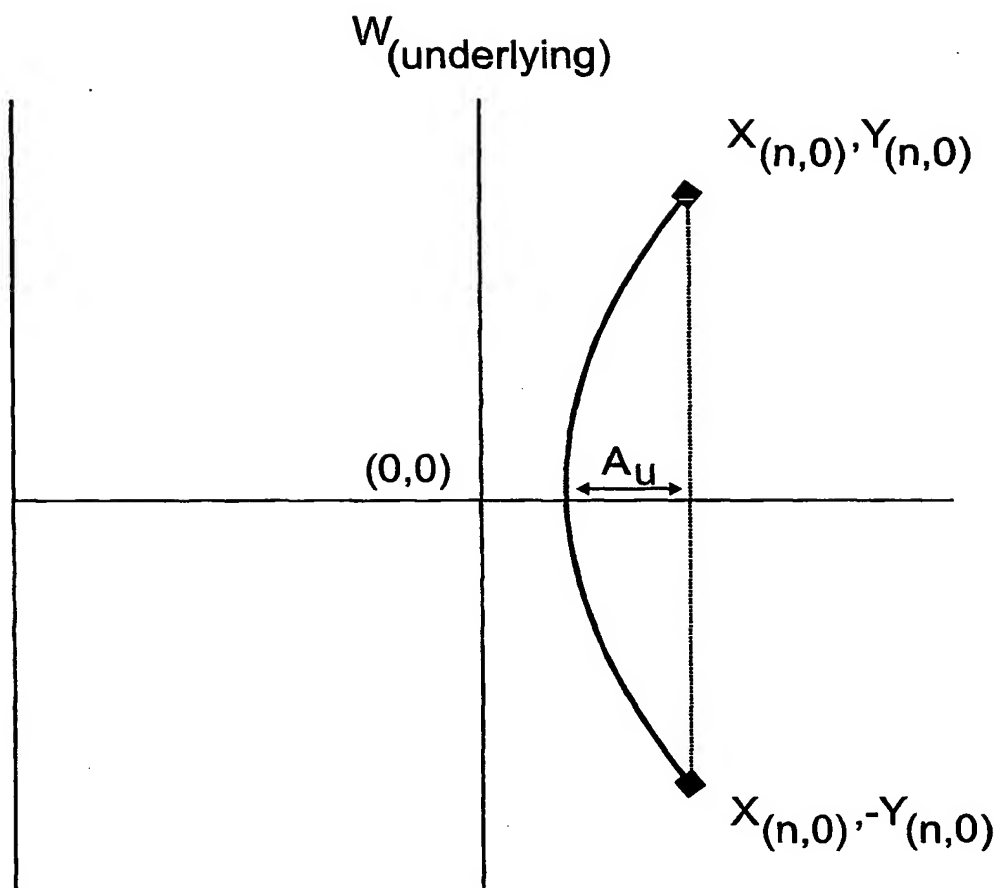
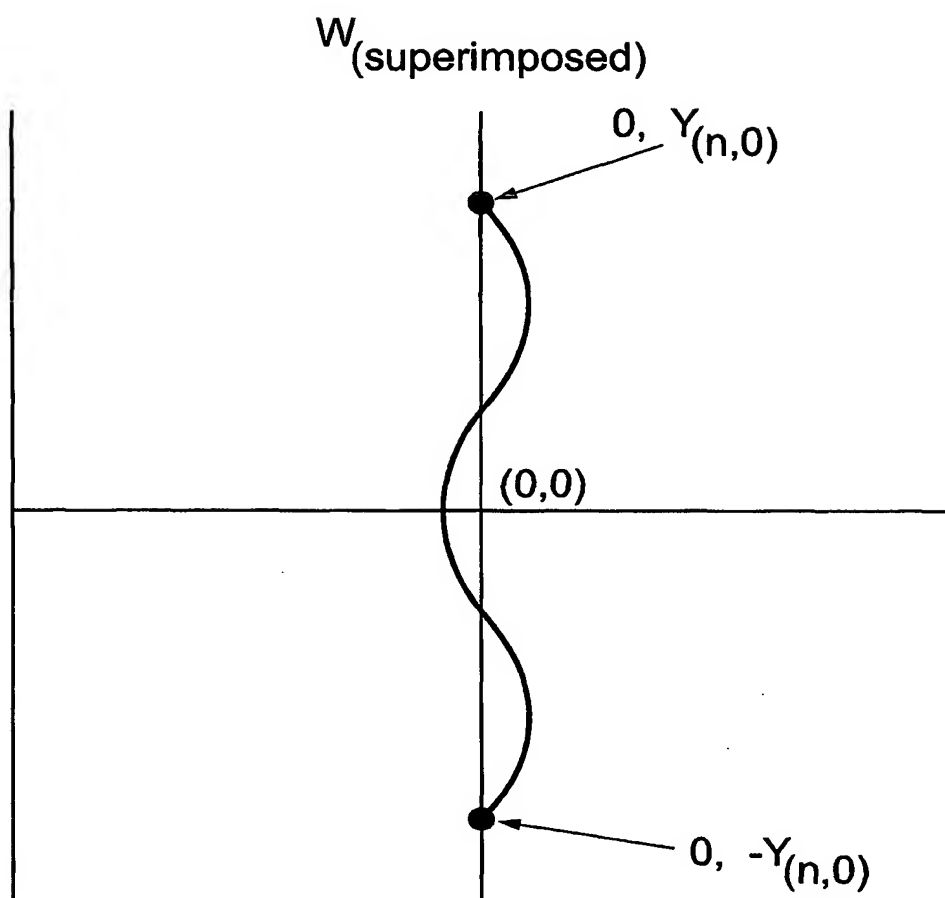


Fig. 15

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*Fig. 16*

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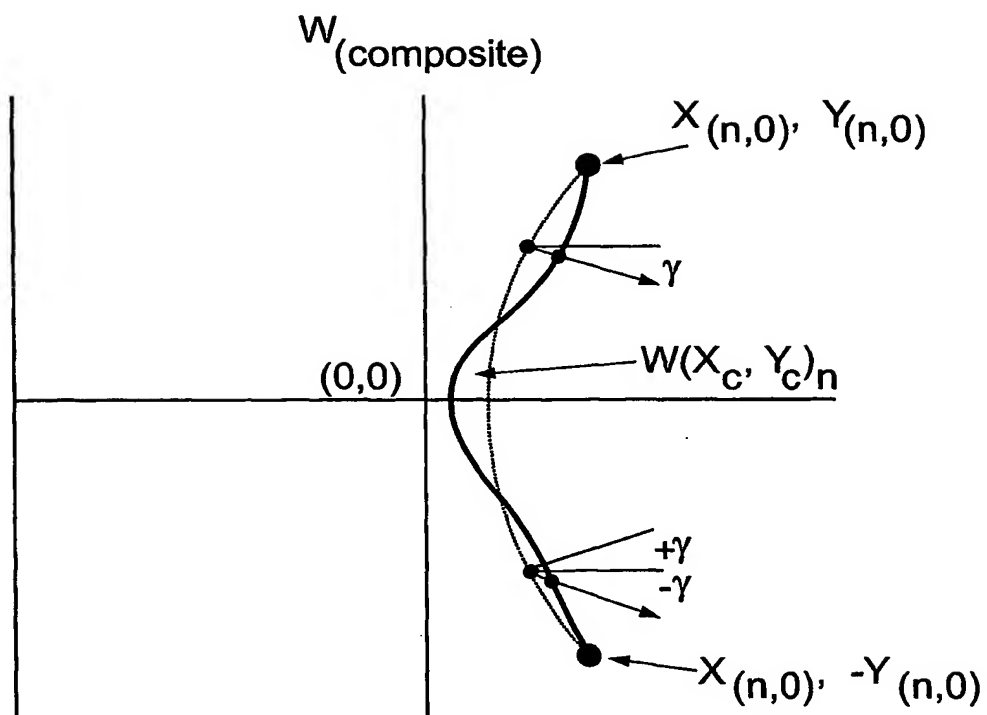


Fig. 17

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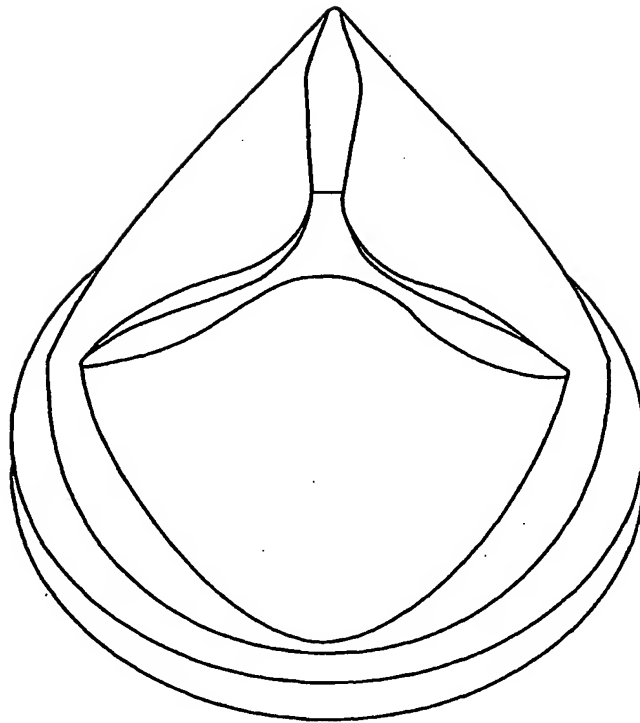


Fig. 18

INTERNATIONAL SEARCH REPORT

Inte nat Application No
PCT/GB 02/02409

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61F2/24

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X A	US 4 364 127 A (PIERCE WILLIAM S ET AL) 21 December 1982 (1982-12-21) column 2, line 5 - line 15 column 3, line 8 - line 10 figures 1-3 ---	1, 10, 14 2, 15
X A	US 6 165 215 A (SONDAK EHAD ET AL) 26 December 2000 (2000-12-26) column 1, line 64 - column 2, line 10 column 4, line 51 - line 55 figures 2, 3 --- -/-	1, 10, 14 2, 15

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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Date of the actual completion of the international search

14 October 2002

Date of mailing of the international search report

22/10/2002

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3018

Authorized officer

Amaro, H

INTERNATIONAL SEARCH REPORT

Int'l Application No
PCT/GB 02/02409

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	<p>WO 01 41679 A (AORTECH EUROP LTD ;WHEATLEY DAVID JOHN (GB); HAWORTH W S (GB); BER) 14 June 2001 (2001-06-14) page 40, line 4 - line 9 claims 1-6,13,15,16,18-20 -----</p>	1-14

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/GB 02/02409

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 4364127	A	21-12-1982	NONE	
US 6165215	A	26-12-2000	AU 6317496 A EP 0897295 A1 WO 9741808 A1 JP 2001501497 T	26-11-1997 24-02-1999 13-11-1997 06-02-2001
WO 0141679	A	14-06-2001	AU 2189401 A EP 1235537 A1 WO 0141679 A1	18-06-2001 04-09-2002 14-06-2001